COCCIDIOIDOMYCOSIS CONTROL PROGRAM

for the

A. A. F. W. F. T. C.

HEADQUARTERS

ARMY AIR FORCES WESTERN FLYING TRAINING COMMAND

Office of the Surgeon

1104 West 8th Street, Santa Ana, California

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ARMY AIR FORCES WESTERN FLYING TRAINING COMMAND
1104 WEST EIGHTH STREET, SANTA ANA, CALIFORNIA
OFFICE OF THE SURGEON

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September 15, 1943

Requests for the syllabus "Coccidioidomycosis Control Program for the WCAAFTC", published in October, 1942, have exhausted the supply of available copies, necessitating this second edition. The text has been completely re-written and some new X-ray reproductions have been added. It is hoped that this presentation on Coccidioidomycosis will aid flight surgeons and Army doctors everywhere in acquiring a practical working concept of the many manifestations of this bizarre disease.

M. G. Healy

M. G. HEALY,
Colonel, Medical Corps,
Surgeon.

HEADQUARTERS
ARMY AIR FORCES WESTERN FLYING TRAINING COMMAND
OFFICE OF THE SURGEON
1104 West 8th Street
Santa Ana, California

710 (Coccidioidomycosis)

SUBJECT: Coccidioidomycosis Control Program for the AAFWFTC

TO: Surgeons, All Stations This Flying Training Command

1. The coccidioidomycosis control officer of this command will visit each of the basic, advanced and specialized schools in the AAFWFTC for the purpose of training medical officers in (1) the detection of sub-clinical cases by standardized coccidioidin skin testing and (2) the diagnosis and treatment of clinical cases of coccidioidomycosis which may develop at the various stations.

2. Each station surgeon will assign one (1) medical officer from the personnel already on duty at his station as a station coccidioidomycosis control officer. The officer chosen will be a key man and one likely to remain at the station indefinitely. If possible, the man selected should be a pediatrician or a physician trained in contagious diseases, so that he may act as epidemiologist and care for all contagious disease outbreaks at the station in addition to his duties in connection with the coccidioidomycosis problem.

3. Each station surgeon will be responsible for the effective execution of the coccidioidomycosis control program at his station. The duties of the station coccidioidomycosis control officer will include:

a. Skin testing with coccidioidin of all:

(1) Enlisted personnel and officers assigned to the station as of 1 November 1942, the results to be noted on each man's immunization register, Form M.D. #81.
(2) Additional enlisted personnel and officers subsequently assigned to the station immediately upon their arrival, and a repeat coccidioidin skin test on all enlisted men and officers on duty at the station twice yearly thereafter for the duration of the war.
(a) during the week of January 1 to 8 and
(b) during the week of July 1 to 8
(3) Enlisted personnel and officers prior to their transfer from each station.
(4) Cadets during their 64 examination prior to their graduation from advanced training courses, the results to be recorded on the 64 record and compared with the results of the first coccidioidin test which will be performed on each cadet during his first week at SAAAB.

b. The diagnosis and treatment of all active cases of coccidioidomycosis, - including coccidioidin skin testing, chest x-ray studies, sedimentation rates, etc.

c. The sending by Air Mail to Dr. Charles Smith, Stanford University School of Medicine, San Francisco, of 10 cc. of whole blood for precipitin and complement fixation reactions from:
(1) Patients with a protracted course and a persistently prolonged sedimentation rate,
(2) Patients with a doubtful prognosis and a possibility of dissemination, and
(3) Cases of serious diagnostic doubt.
These blood specimens will be sent in containers, especially provided each field by the coccidioidomycosis control officer of the AAFWFTC, accompanied by a brief clinical abstract including statement as to past residence in endemic area, date of onset and any outstanding clinical symptoms such as erythema nodosum, state of coccidioidin sensitivity, etc.

d. Sending a clinical epidemiological summary of each new patient with the diagnosis of coccidioidomycosis to the control officer at AAFWFTC on forms provided by this office.

e. The monthly reporting to the coccidioidal control officer at AAFWFTC of all:
(1) Coccidioidin skin testing, - the number of tests performed and the names, rank, organization, etc. of all those with positive reactions.
(2) Hospital cases including:
(a) New cases of coccidioidomycosis occurring during the month since the previous report.
(b) Old cases previously reported but still on the wards, and
(c) The total number of hospital days spent during the month by patients with proved diagnosis of coccidioidomycosis.

4. Each cadet arriving at SAAAB should be skin tested with coccidioidin and the results noted on the 64 examination record for comparison with the repeat coccidioidin skin test to be done at the time of the cadet's graduation from advanced training. This information will be most helpful in those cadets who may develop clinical coccidioidomycosis during their training period. A negative coccidioidin test at SAAAB, for instance, and later a positive skin test during an acute illness in one of the endemic areas, would be significant.

5. Seriously ill patients with a diagnosis of coccidioidomycosis or patients who have had clinical evidence of an active infection for a protracted period (over three months) will be transferred from the various station hospitals to the hospital at SAAAB for further study.

6. Such a program will be helpful (1) in obtaining more accurate information concerning the incidence of coccidioidomycosis in the various stations, this Command; (2) in effecting early diagnosis of active cases of coccidioidomycosis and continuing treatment sufficiently long to prevent

dissemination; and (3) in accumulating data through routine coccidioidin testing of all cadets, enlisted personnel and officers in the AAFWFTC which later may aid the Veterans' Bureau in the disposition of possible claims against the government.

M. G. HEALY
Colonel, Medical Corps
Surgeon

3 Incls:
1- Coccidioidal infection report, AAFWFTC (Blank Form)
2- Monthly Report
3- Syllabus on Coccidioidomycosis

Note:-

The Army Air Forces Western Flying Training Command is grateful to Dr. Charles E. Smith of the Stanford University School of Medicine for his invaluable assistance in establishing the coccidioidomycosis control program and to Dr. R. A. Carter, roentgenologist of the Los Angeles County Hospital, for permission to reproduce some of his films showing the bone lesions of progressive coccidioidomycosis.

HEADQUARTERS
ARMY AIR FORCES WESTERN FLYING TRAINING COMMAND R-ell
OFFICE OF THE SURGEON
1104 West 8th Street
Santa Ana, California

WC 710 (Coccidioidomycosis)

SUBJECT: Coccidioidomycosis Control Program

TO : Surgeon, All Basic, Advanced and Specialized Schools of the AAFWFTC (Attention: Coccidioidomycosis Control Officer)

1. In accordance with directive dated October 16, 1942 which was included in the syllabus on Coccidioidomycosis, you will send monthly reports as of the last day of each month, to reach this office not later than the fifth day of the following month, concerning the activities of the Coccidioidomycosis Control Officer. These reports should include data on:

(a) Coccidioidin skin tests of:
(1) Officers and
(2) Enlisted personnel assigned to your post as of November 1, 1942, the testing to be done now. All additional officers or enlisted men assigned subsequently to that date should be tested within 48 hours after their arrival at your field.
(3) Repeat coccidioidin skin testing of:
(a) Officers and enlisted men on duty at your post, twice yearly thereafter, the testing to be done during the weeks of January 1 to 8 and July 1 to 8.
(b) Officers and enlisted men prior to their transfer from your field.
(c) Cadets during their 64 examination prior to graduation from Advanced Training Schools, the results to be recorded on their 64 record. Each new Cadet arriving at SAAAB will be skin tested with coccidioidin during his first 64 examination. If the "repeat" coccidioidin test is positive, include report of the SAAAB coccidioidin test in your summary for comparison.
The skin tests should be read 44 to 48 hours after the intracutaneous injection of 0.1 cc of 1:100 dilution of coccidioidin. The reactions should be interpreted thus:

/) Definite induration and erythema, but less than 1cm in diameter.
// Induration of 1cm in diameter
/// Induration of 1cm in diameter plus flare of erythema of 1cm or more
//// Induration of 2cm or more
//// Vesiculation.

2. Seriously ill patients with a diagnosis of coccidioidomycosis or patients who have had clinical evidence of an active coccidioidal infection for a protracted period (three months or more in hospital) should be transferred from the various station hospitals at the basic, advanced and special-

ized schools to the station hospital at SAAAB for further study.

3. The coccidioidin testing material, tuberculin syringes, platinum needles, rubber stamps for reporting ("coccidioidin, positive" and "coccidioidin, negative") report blanks, etc. will be supplied by Office of the Surgeon, Hdqrs., AAFWFTC, Santa Ana, California.

M. G. Healy

M. G. HEALY
Colonel, Medical Corps
Surgeon

2 Incls:
(1)- Sample Copy, Monthly Report
(2)- Sample Copy, Coccidioidal Infection Report

HEADQUARTERS
ARMY AIR FORCES WESTERN FLYING TRAINING COMMAND
OFFICE OF THE SURGEON
1104 West 8th Street
Santa Ana, California

BHB:sir

710

SUBJECT: Concerning Laboratory Procedures in the Diagnosis of Coccidioidomycosis.

TO : The Surgeon, All Schools Except Army Air Forces CTD'S, This Training Command (Attention: Coccidioidomycosis Control Officer).

1. Sputum examinations -

Routine sputum studies are not indicated in patients suspected of having coccidioidomycosis because:

a. Most patients do not cough sufficiently to raise adequate amounts of sputum for examination.

b. Failure to recover the fungus from sputum does not rule out the possibility of infection.

c. Carefully carried-out sputum studies are both tedious and expensive. Further, short-cut methods, such as a cover-slip examination, are not dependable, and,

d. Other procedures, especially determination of precipitins and the complement fixation titre, are more accurate in the event that the diagnosis of coccidioidomycosis cannot be made on the basis of history, clinical picture, characteristic chest X-ray and an elevated sedimentation rate.

2. Blood specimens for determination of precipitins and complement-fixation titre -

Blood specimens should be sent, by Air Mail if possible, to Dr. Charles Smith, Stanford University School of Medicine, San Francisco, Specimens should be sent in sterile bottles, previously autoclaved, and in special containers, both of which will be supplied thru the office of the Coccidioidomycosis Control Officer, AAFWFTC. No attempt should be made to separate the blood cells from the serum.

Blood specimens for the determination of precipitins and the complement fixation titre should be sent only from:

a. Patients with a protracted course and a persistently prolonged sedimentation rate.

b. Patients with a doubtful prognosis and a possibility of dissemination and

c. Cases of serious diagnostic doubt.

3. Coccidioidin dilutions for skin testing -

All routine coccidioidin testing should be done with a 1:100 dilution of coccidioidin. However, hospital patients who present skin lesions (erythema nodosum, erythema multiforme, etc.) and who are suspected of having coccidioidomycosis, should be tested initially with a 1:1000 dilution, because of the unusual sensitivity to coccidioidin in such instances. If this first test is negative, a second test, using a 1:100 dilution of coccidioidin, is indicated before ruling out the disease in the differential diagnosis.

4. Positive reactors to coccidioidin skin tests -

During the course of routine coccidioidin skin testing, all men who show:

a. a 3 plus or a 4 plus reaction on the initial test or

b. a definitely positive reaction (1 plus thru a 4 plus) on re-testing, (having previously shown a negative coccidioidin reaction) should have a sedimentation rate determination, and an X-ray of the chest, if the sedimentation rate is appreciably above 12 mm.

A normal sedimentation rate (12 mm. or below by the Cutler method) and a negative chest X-ray, in the presence of a positive coccidioidin skin test, indicate a previous coccidioidal infection which has completely healed by the time the test was performed.

Those patients with evidence of activity (increased sedimentation rate, characteristic chest X-ray and suggestive clinical symptoms and findings) should be hospitalized.

For the routine re-testing of personnel on duty at your post during the weeks of January 1 to 8 and July 1 to 8, it will be unnecessary to re-test those individuals who reacted positively to coccidioidin with previous tests.

5. Monthly reports of positive reactors -

The monthly reports of positive reactors to coccidioidin skin tests should be listed in the order of the severity of the skin reaction, beginning with 4 plus, then 3 plus, 2 plus, 1 plus and ending with the plus-minus reactions.

The residence of each positive reactor, or the probable state in which the infection was acquired, should be listed in addition to his name and ASN.

6. These instructions are considered by the Surgeon to be a supplement to the pamphlet on Coccidioidomycosis Control and one (1) copy will be inserted in that publication on file at your station.

M. G. Healy

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Colonel, Medical Corps,
Surgeon.

MONTHLY REPORT - COCCIDIOIDOMYCOSIS CONTROL PROGRAM

STATION: _____ DATE OF REPORT _____

SECTION ONE

COCCIDIOIDIN SKIN TESTING (upon arrival at this Post)	TOTAL NUMBER OF TESTS	TOTAL NUMBER OF POSITIVE TESTS
Officers:	_____	_____
Enlisted Personnel:		
White:	_____	_____
Colored:	_____	_____

SECTION TWO

REPEAT COCCIDIOIDIN SKIN TESTING

Officers: (Semi-annually only or prior to transfer from Post)	_____	_____
Enlisted Personnel: (Semi-annually only or prior to transfer from Post)		
White:	_____	_____
Colored:	_____	_____
Cadets: (By classes at final 64 exam)		
Class_____Grad. Date_____	_____	_____
Class_____Grad. Date_____	_____	_____

SECTION THREE

	NUMBER WHITE	NUMBER COLORED
a. New patients since previous report. (Report each new patient on special blank)	_____	_____
b. Patients previously reported but still in hospital on date of report.	_____	_____
c. Total number of hospital days during current month for all patients with coccidioidomycosis	_____	_____
d. Name, Rank, A.S.N., Organization, etc. of all personnel, except cadets, with positive tests, should be listed in the order of their degree of reaction, i.e., ////: ///: ##: /.	_____	_____

STATION_____ DATE:_____

COCCIDIOIDAL INFECTION REPORT, AAFWFTC

Name_____ Age_____ Nationality_____

Rank & Organization_____ Birthplace_____

Residence in: (How long in each and when?)

Texas_____ New Mexico_____ Arizona_____

California (what sections)_____

Other states_____

Previous Army Assignments: (List states and how long there)

_____

When did patient arrive at this field_____

Present Illness (Dates)

Headache	Cough	Malaise	Joint Pains
Conjunctivitis	Anorexia	Chill	Backache
Night Sweats	Nervousness	Fever	Pleurisy

Skin Lesions (description)

Other symptoms:

_____

Dates: 1st Dispensary visit_____ Hosp. Admission_____

Discharge_____

Physical Examination (Date) _____

Temperature_____

Chest Examination _____

Skin Lesions_____

Other findings:_____

X-Ray Findings (Date)_____

_____

Laboratory Findings and dates:

W.B.C. and differential:

Sedimentation rate:

Precipitins:

Complement Fixation:

Coccidioidin Tests: (Dates and readings)

Course: (Use other side for details, if necessary) _____

M.C.

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SYLLABUS ON COCCIDIOIDOMYCOSIS

Definition

Coccidioidomycosis, an infection caused by the fungus Coccidioides immitis, occurs in two forms: (1) primary coccidioidomycosis, an acute, benign, self-limited respiratory infection; and (2) progressive coccidioidomycosis, a chronic, disseminated, usually fatal disease, which is manifested by cutaneous, subcutaneous, visceral, and osseous lesions.

Historical Data

Coccidioidomycosis was first observed and reported in 1892 by Posadas and Wernicke in South America. In 1894 Rixford reported the first case in the United States, a patient from the San Joaquin Valley of California, with a severe, fatal, generalized granulomatous infection. Later Ophuls and Moffitt gave the first adequate description of the fungus. Subsequent to Rixford's famous case, other patients with similar findings, granulomata of skin, bones, joints and various organs, were seen from time to time, most of them originating in the San Joaquin Valley. It soon became apparent, however, that other regions adjacent to the San Joaquin Valley were also points of origin.

For 40 years disseminated coccidioidomycosis was the only known form of this disease. In 1935, however, Gifford and Dickson observed a similarity between the prevalent "valley fever" or "desert rheumatism" and coccidioidal granuloma, as it was then called, and demonstrated that Coccidioides immitis is the etiological agent in both conditions. Dickson proposed the terms primary and secondary coccidioidomycosis to designate the two types of this disease. Since then a considerable literature has accumulated with the work of C. E. Smith, of Stanford University Medical School, and at present consultant for the Secretary of War, especially contributing to our knowledge of this disease.

Epidemiology and Etiology

The chief endemic foci are the southern part of the central valley (San Joaquin) of California, southern Arizona, and western Texas. Another known focus is San Benito County of California, while occasional cases have been reported in Idaho, southern Utah, southern California, and New Mexico. Outside the United States coccidioidomycosis has been observed infrequently in Mexico, Hawaii, and Italy, as well as in Uruguay, Bolivia, Argentina, and Brazil. Coccidioidin testing of military personnel who have served in dusty regions of Australia, northern Africa, the Near East, etc. may indicate a more universal distribution of the fungus than has heretofore been realized.

In the endemic regions the climate is hot, dry, and dusty, with the highest incidence of acute infections occurring during the dry summer and fall months. A definite correlation has been observed between the number and severity of dust storms and the incidence of new cases of coccidioidomycosis in endemic areas. Inhalation of spore-laden dust from hay, produce, and other products from endemic areas, as well as dust on clothes and motor vehicles which have been transported a considerable distance from these regions, has caused the disease in susceptible individuals.

Because man and many animals apparently become infected only by the inhalation of dust which contains the chlamydospores of Coccidioides immitis, some reservoir, such as the soil, or a living host, plant or animal, must exist in endemic areas, thereby providing for the propogation and dissemination of the fungus. If the fungus grows in soil, few susceptible animals, especially those living in burrows in infested ground, should escape infection. However, Emmons trapped many soil-dwelling rodents in widely separated areas of Arizona, and demonstrated that only certain species, principally pocket mice and kangaroo rats, constitute a probable reservoir for the disease. In the lungs of these infected animals, this investigator found typical coccidioidal lesions from which Coccidioides immitis was cultured. Similar species of rodents, trapped in a part of New Mexico where coccidioidomycosis is not endemic, did not show these changes. Emmons isolated another fungus, Haplosporangium parvum, from even a greater percentage of desert rodents in Arizona, and suggested that this fungus may be related etiologically to Coccidioides immitis, inasmuch as some individuals with a positive coccidioidin test also react positively to skin testing material prepared from Haplosporangium parvum.

Coccidioidomycosis is most common in newly arrived residents in endemic areas. A large proportion of the population of these regions will react positively to coccidioidin skin tests, indicating previous infection. The percentage of positive skin tests will vary from 10% to 30% of those who have resided less than a year in the area to at least 75% of those who have lived there for ten years or more. All age groups are susceptible, although male adults with occupational exposure to agricultural dust are most likely to develop infection. The disease tends to disseminate much more frequently in men than in women. The dark-skinned races, especially negroes, Filipinos, Mexicans, and Orientals, have a greater susceptibility to coccidioidal infections, in addition to a greater tendency to develop the disseminated or progressive form of the disease than have the white races.

The Causative Agent.

Coccidioides immitis usually is grouped with the fungi imperfecti. In tissue the parasite causes a granulomatous reaction with a tendency to central caseation or suppuration. In purulent exudate, in particular, the fungus often appears in remarkable abundance. It is a spherical structure, varying from 5 to 80 microns in diameter, with an average of 30 microns. As the spherule develops, the capsule thickens and becomes more refractive. The very coarsely granular protoplasm contained therein breaks up into a large number (50 to 100) of spores of irregular shape and only a few microns in diameter. With rupture of the capsule these minute bodies are discharged into the tissue, where they swell, become spherical, and grow until they reach the sporulating stage.

On solid media the fungus develops in a few days, even at room temperature, as a fluffy white mass composed of irregularly arranged branching septate filaments 2-8 microns in diameter. The appearance of cultures varies with age, temperature, and nutrient conditions. In contrast to the endosporulation seen in tissue, the organism reproduces in culture by budding and fragmentation of the mycelium. Pieces of dead wood, strips of cactus, potatoes, and other vegetables, are favorable to its growth. The organism is resistant to drying, and dry cultures are an obvious laboratory hazard. Most laboratory personnel who work with Coccidioides immitis invariably acquire the infection by inhaling the almost imperceptible dust of the mycelia while working with cultures. Details of the transitions between the spherule and mycelial stages are incomplete, and almost nothing is known of the existence of the fungus in nature where it has never been observed directly. It has been described as an agent of spontaneous infection in a variety of animals, but such infections are rare. Attempts to cultivate the fungus from soil in endemic areas have proved almost entirely futile, although isolation from soil by animal inoculation has been more successful.

Although the spherule is infectious, no proved instance of man to man, animal to animal, or animal to man transmission has been recorded. Guinea-pigs have been infected experimentally at Santa Ana Army Air Base by inoculations of extracts of dust from rooms in which patients dying of disseminated coccidioidomycosis have been housed. This would indicate that the chlamydospores may develop in cracks and crevices in the floors and walls, and might serve as a potential source of infection for other patients in the ward. The danger, however, seems remote and can be obviated by daily lysolizing of the floors, etc. in rooms housing these patients.

Pathogenesis.

As in tuberculosis, coccidioidal infection usually occurs by inhalation of the specific agent after an incubation period of ten to fourteen days. Only in endemic areas, however, is the air contaminated with the chlamydospores of Coccidioides immitis, and in these areas the disease is prevalent chiefly during the hot and dusty months. A history of skin abrasion, puncture wound, or other trauma sometimes precedes certain rare instances of chronic infection, the fungus being introduced directly into the subcutaneous tissues. Old pulmonary lesions containing typical spherules have been observed in patients dying of other causes. After lying dormant for many years such lesions might conceivably flare up and result in a disseminated infection and death. Only one such instance, however, is on record.

The disease is unlike tuberculosis in that the initial infection usually confers permanent immunity against subsequent reinfection. Even though residents in endemic areas, such as the San Joaquin Valley in California and southern Arizona, continue to be exposed to repeated inhalations of infected dust throughout their lives, the incidence of progressive coccidioidomycosis is extremely low, probably no more than one patient with the disseminated form to every five hundred cases of the benign, primary coccidioidomycosis.

As our knowledge of the disease has increased, the diagnosis of primary coccidioidomycosis has been made with greater frequency. In most patients, however, the infection still is not recognized clinically, the symptoms being attributed to a cold or an influenzal infection. Further, it is probable that many patients acquire the infection without showing clinical symptoms or findings during any stage of the disease other than the subsequent positive reaction to coccidioidin.

In the clinically recognized patient with coccidioidomycosis, varying degrees of pneumonitis, sometimes associated with hilar adenopathy, is a common finding. This primary focus apparently is walled off, as in tuberculosis, and most often undergoes complete resolution, sometimes, however, with fibrosis and calcification resulting. In some of the nodular parenchymal lesions, necrosis occurs with the production of a small, thin-walled cavity. Usually there is only one such lesion, although multiple cavities have been observed. Any area of the lung can be involved. The absence of surrounding parenchymal reaction is a characteristic feature of coccidioidal cavitation. During the many months which usually elapse before complete closure is evident by X-ray, the cavity serves as a reservoir for the growth of Coccidioides immitis. Apparently, however, there is little danger of dissemination during this time or subsequently. Although the patient's sputum may contain the fungus or blood, as there may be hemorrhages of varying degree in some patients, the coccidioidal cavity is usually silent. Further, a normal sedimentation rate, a low titer or disappearance of complement fixation, and absence of fever and constitutional symptoms indicate that the infection is inactive and well focalized. Coccidioidal cavitation usually always represents a part of a primary infection.

Occasionally primary coccidioidomycosis is manifested by a primary pleural effusion, similar to that seen in tuberculosis. Coccidioides immitis may be recovered from the fluid. Within a comparatively short period the fluid usually disappears completely, leaving a slight pleural thickening as the only residual evidence of infection.

In contrast to the benign nature of the primary infection is the seriousness of the disseminated or progressive form of coccidioidomycosis. In most instances death occurs after a prolonged course of many weeks up to six months or more, during which time the fungus disseminates throughout the body in a manner somewhat suggestive of miliary tuberculosis. It must be remembered, however, that an occasional patient with progressive coccidioidomycosis will focalize his infection, usually after a prolonged period of bed rest, and make a complete recovery. This progressive type of coccidioidal infection is not "secondary," as is implied in the usual classification ("primary" and "secondary") of the two forms of this disease. It occurs in certain individuals as one continuous, progressive disease, although the serious form may not be recognized as such until several weeks or months have elapsed after the infection first becomes evident.

Symptomatology of Primary Coccidioidomycosis.

Many cases of primary coccidioidomycosis are subclinical and can be detected only by a positive coccidioidin skin test. After an incubation period of ten to fourteen days, those with clinical manifestations run a

low grade fever (usually 99° - 101°) which sometimes is associated with chills, night sweats, anorexia, backache and headache. A non-productive, brassy cough may be present, although most patients will raise small amounts of muco-purulent sputum which occasionally is blood-streaked. More characteristic, when it occurs, is the chest pain which some patients describe as a sensation of constriction in the upper chest, while others complain of sharp pleuritic pains which may be mistaken for coronary occlusion, fractured ribs, or nephrolithiasis. These initial symptoms represent the acute respiratory phase which subsides usually in one to two weeks.

In 3% of the cases, a second phase follows in from three to twenty-one days, during which fever recurs and erythema nodosum, similar to that seen in primary tuberculosis, is a prominent finding. Usually the lesions of erythema nodosum are most marked on the shins, but in some patients they occur on arms, thighs, buttocks, and scalp. Within two to three days the marked tenderness subsides and the lesions begin to fade, leaving only a brownish pigmentation which may persist for weeks. In rare instances a secondary crop of erythema nodosum occurs after an interval of some weeks. Lesions of erythema multiforme also may appear on the margins of the palms, the face, neck, and upper extremities at the same time, with or without erythema nodosum. Patients with erythema nodosum or multiforme are least likely to develop the progressive form of the disease.

Other occasional findings are phlectenular conjunctivitis and acute arthritis, with the knees and ankles most likely to be involved. The joints are tender on pressure and painful on motion, but usually not as edematous as in rheumatic fever. The dramatic response to large doses of salicylates is usually lacking in coccidioidal arthritis, providing a helpful point in differential diagnosis.

For the most part, however, patients with primary coccidioidomycosis rarely appear or feel ill. A visitor in the coccidioidomycosis wards in station hospitals of the AAFWFTC, such as those at Minter, Lemoore, Luke and Williams Fields, usually is impressed with the appearance of well-being in most of the coccidioidal patients. This is born out by the average patient's most frequent question: "Why must I stay in bed when I feel so well?"

Physical examination at the onset of acute coccidioidomycosis reveals few significant findings other than a low grade fever. A mild naso-pharyngitis may be evident, but usually this represents a coincident infection during the early stages of the disease. Only occasionally, even when pleuritic pain is present, can slight suppression of the breath sounds, dullness and rales be demonstrated. An X-ray of the chest, however, will show one or more of the characteristic changes in at least four out of every five patients. These X-ray changes usually consist of (1) soft, fuzzy hilar thickening, (2) pneumonia-like infiltrations, (3) nodular parenchymal lesions, or (4) mediastinal and hilar adenopathy. (See section on The Roentgen Diagnosis of Coccidioidomycosis).

Residual pulmonary coccidioidal cavitation is an infrequent complication of acute coccidioidomycosis and is demonstrable only by X-ray, there being no symptoms other than occasional hemoptysis and sometimes spherule-laden sputum. However, coccidioidomycosis must be considered whenever pulmonary cavitation occurs in a patient with negative tuberculin tests and no demonstrable

tubercle bacilli in his sputum. Because the coccidioidal cavity occurs in one of the areas of consolidation, it is not evident for at least several months after the onset of the infection in most instances. When the cavity is diagnosed the infection usually is well focalized as indicated by a normal sedimentation rate together with a low titer or complete absence of complement fixation in the patient's serum. Although these cavities eventually close spontaneously, a continuous rest regime will hasten complete healing of the pulmonary lesion.

Erythema nodosum occurs in only 3% of patients with primary coccidiodomycosis. The lesions appear as well-defined, red, tender nodules of various sizes, usually on the extensor surfaces of the legs and arms. Patients with erythema nodosum always show a markedly increased sensitivity to coccidioidin. Occassionally erythema multiforme is present with symmetrically distributed macules, papules, or vesicles on the face, neck, or extensor surfaces of the extremities.

Symptomatology of Progressive Coccidioidomycosis.

In direct contrast to the benign nature of primary coccidioidomycosis is the seriousness of the progressive form of the disease, which sometimes is referred to as "secondary coccidioidomycosis," "coccidioidal granuloma," "San Joaquin Valley Fever," "California Disease," or "desert fever."

Fortunately, the incidence of dissemination is extremely low, probably not more than one patient in five hundred failing to combat successfully the initial infection. Actually the patient with progressive coccidioidomycosis shows evidence of dissemination within a few weeks or months after acquiring the infection. His clinical picture at first is similar to that of primary coccidioidomycosis. Without a let-up, however, the initial symptoms and physical findings continue with the sedimentation rate remaining elevated, the serology revealing an increase in the titer of both precipitins and complement fixation, and X-rays revealing further extension of lung infiltration. In some instances, involvement of bones and joints, lymph nodes, skin and meninges become apparent.

These patients with progressive coccidioidomycosis run a slow, down-hill course lasting from a few months to a year or more in some instances. In those cases in which the pulmonary pathology predominates, low grade fever, cough, spherule-laden sputum, marked weakness, and loss of weight are prominent symptoms. As the end approaches the cyanosis and dyspnea are pronounced, being proportionate to the degree of lung infiltration. So little normally functioning lung tissue remains in such patients that anoxia appears to be the principal factor in the immediate cause of death. Patients with generalized miliary dissemination usually have high fever, chills, profuse sweats, and become emaciated due to progressive loss of weight. Large subcutaneous abscesses, containing a creamy purulent material filled with spherules, are a frequent finding in addition to deeper abscess formations, which in most instances are first discovered at autopsy. Arthritis is an occasional finding, with the involved joints becoming red, somewhat swollen, and painful. Some destruction of the adjoining bone is demonstrable by X-ray. Any bone of the body may become involved in progressive coccidioidomycosis with cyst-like areas of bone destruction, usually in the calcellous bone, and periostitis the most characteristic lesions. Throughout the entire

course of the disease, even in those patients with the most extensive pulmonary pathology, the physical findings are far less prominent than the degree of involvement would suggest.

Just why approximately 499 of every 500 patients with primary coccidioidomycosis can control the infection within a few weeks time in most instances, while the remaining patient disseminates during many weeks or months, with death usually resulting, is not known. However, such factors as racial, sexual, and individual resistance seem important. Especially is this true in negroes and other pigmented patients who disseminate much more frequently than do white patients with coccidioidal infections. So far the only deaths in the AAFWFTC have occurred in seven negro patients, while the actual incidence of primary coccidioidomycosis in negroes stationed in this command has been approximately three to four times greater than in white soldiers.

Diagnosis.

Primary coccidioidomycosis is sometimes mistaken for influenza or pneumonia, while the progressive form of the disease may be confused with tuberculosis. Especially is this true in those patients with coccidioidal meningitis in whose spinal fluid the spherules are as difficult to demonstrate as are the tubercle bacilli in tuberculous meningitis. Inasmuch as the chest X-ray may show the "snow storm" appearance of miliary dissemination or other comparable findings in both diseases it is necessary to establish the diagnosis of definite coccidioidal infection by laboratory procedures. The bone lesions also may be similar in coccidioidal infections and tuberculosis. Other mycotic diseases may produce symptoms and findings similar to coccidioidomycosis. Haplosporangium parvum, especially, may cause confusion, inasmuch as many patients with proved coccidioidomycosis in Arizona hospitals also reacted positively to an antigen made from this fungus which apparently is also endemic in that state.

Some form of laboratory confirmation is necessary in making the diagnosis of coccidioidomycosis. In most cases with a suggestive history, as well as characteristic physical and X-ray findings, only a positive coccidioidin skin test and an elevated sedimentation rate are necessary. In some instances, however, the fungus must be demonstrated either in tissue sections or by culture of sputum and exudates with subsequent animal inoculations. Testing the patient's serum for precipitins and complement fixation, using coccidioidin as antigen, is extremely helpful in making the diagnosis in doubtful cases, in addition to aiding in the early discovery of those patients in whom the fungus infection is most likely to disseminate.

The coccidioidin skin test is as important in the diagnosis of coccidioidomycosis as the tuberculin test is in tuberculosis. In the AAFWFTC coccidioidin is used which is prepared at Stanford University School of Medicine by growing many strains of coccidioides on Bureau of Animals Industry asparagine medium for one to two months. The material is tested for potency and specificity on previously infected, as well as normal, individuals before being released for clinical use. Undiluted coccidioidin remains potent for at least three to four years, while a 1:100 dilution in normal saline is satisfactory for skin testing for one to two months if kept refrigerated. The skin test is performed in the same manner as is the Mantoux

test for tuberculosis. For routine testing, 0.1 cc of a 1:100 dilution of coccidioidin is injected intradermally on the right forearm, and the test is read in 48 hours. The consistent use of the right forearm for coccidioidin testing and the left forearm for tuberculin testing will avoid confusion in the interpretation of results. A special "tuberculin syringe" should be used for this test exclusively. False positive reactions are likely if the same syringe is used for tuberculin and other tests as well as for coccidioidin skin testing. A positive test will show a reaction of more than 0.5 cm. in diameter, with erythema, induration, and sometimes vesiculation. Usually the local reaction to coccidioidin is considerably more pronounced than is a corresponding reaction to old tuberculin in a proved tuberculous patient. In spite of an occasional violent skin reaction, which may cover the entire forearm, there is little danger to the patient of dissemination or of reactivating an old, arrested process.

A positive test is usually recorded 1 plus, 2 plus, 3 plus, or 4 plus, according to the degree of reaction. However, the size of the local reaction represents the patient's allergic response to coccidioidin and is not a measure of present activity. A positive test, therefore, regardless of the size of the local reaction, may indicate either an old infection acquired many years previously, or a recent and active involvement. However, a change-over from a previously negative reaction to a positive skin reaction to coccidioidin is extremely helpful in making the diagnosis of active coccidioidal infection.

Since October, 1942, every aviation cadet who received his pre-flight training at Santa Ana Army Air Base has been skin tested and the results "Coccidioidin positive" or"Coccidioidin negative" noted at the top of his "64" examination record. Approximately 5% of these men have reacted positively, indicating residence in an endemic area and a primary infection previous to beginning cadet training at Santa Ana. Subsequent coccidioidin testing of every squadron prior to graduation from an advanced school has revealed positive reactions in an additional 10% indicating coccidioidal infection, which may or may not have been recognized clinically, at some time during their months of actual flight training. This figure includes all cadets, many of whom were trained at various fields in the AAFWFTC which are not in coccidioidal endemic areas. The infection rate, as indicated by a change-over from a negative to a positive coccidioidin test, is much higher in cadets trained at fields in the San Joaquin Valley (Minter, Lemoore, and Gardner especially), in central and southern Arizona (Luke, Williams, and Yuma especially), and in western Texas (Pecos and Marfa especially). Retesting of officers and enlisted personnel stationed in those areas for a year or more has shown a change-over to a positive coccidioidin test as high as 30% at some of these fields.

The <u>significance of the test</u> is comparable to that of the tuberculin test. Just as a positive tuberculin test indicates a sensitivity to tuberculin, a positive coccidioidin skin test indicates sensitivity to coccidioidin, due to a present or a past infection, but does not necessarily mean that an active infection exists at the time the test is performed. The majority of patients who have recovered from primary coccidioidomycosis will continue to react positively to subsequent skin tests for the remainder of their lives. A positive coccidioidin test is significant of clinical coccidioidomycosis in the presence of a suggestive history, physical signs,

and laboratory findings, particularly in patients who at some previous time may have shown a negative reaction to coccidioidin. A negative skin test in a patient with other findings suggestive of the disease is not conclusive; another skin test, using the same dilution (1:100) should be performed seven to ten days later. Coccidioidomycosis patients with erythema nodosum are unusually sensitive to coccidioidin, showing a markedly positive skin test. On the other hand, patients in the advanced stages of progressive coccidioidomycosis may not react to coccidioidin even when a 1:10 dilution is used, just as a patient with miliary tuberculosis may not react to the usual dilutions of old tuberculin or purified protein derivative. In the routine testing of military personnel, many men from Michigan, Illinois, Iowa, Ohio, Indiana, Kentucky, West Virginia, Pennsylvania, and parts of Texas have shown a false positive reaction to coccidioidin. In none of these states is there a known endemic area for this disease, but the plus-minus reaction may indicate a cross sensitivity to other fungus infections which are endemic in those sections of the country.

The sedimentation rate is helpful (1) in evaluating the significance of a positive coccidioidin test, patients with either primary or progressive coccidioidomycosis almost always showing an elevated rate, and (2) in making a prognosis. A continuously high sedimentation rate is present in most patients with progressive coccidioidomycosis, while the originally elevated rate gradually returns to normal (below 12 mm by Cutler method) as the process is arrested in patients with the primary form of the disease. In addition, this test is a fairly accurate therapeutic guide, for the coccidioidal patient should be kept on a bed rest regime until the sedimentation rate is consistently normal.

The blood count usually shows an initial leukocytosis with a marked increase in the number of eosinophiles in some instances early in the course of the disease. In progressive coccidioidal infections, even during the days prior to death, the blood counts are not significant except for an iron deficiency anemia.

Coccidioidin serological tests have proved an extremely useful and accurate diagnostic and prognostic aid. Using coccidioidin as antigen, the patient's serum may be tested for precipitins and complement fixation in (1) doubtful cases, (2) in patients with a protracted course and a persistently prolonged sedimentation rate, and (3) in patients with a doubtful prognosis due to the possibility of dissemination. The tests usually are negative in the very mild infections. In more severe infections, however, precipitins are present in fairly high dilutions with the titer of complement fixation directly proportionate to the degree of the coccidioidal involvement. A rise in titer of complement fixation or the maintenance of a positive reaction at high levels indicates dissemination of the infection. As patients recover from primary coccidioidomycosis these tests become negative, although in some instances, in cavity cases especially, serum may fix complement in low dilutions for many months following clinical recovery. On the other hand, a patient with a large coccidioidal cavity, demonstrable by X-ray, may show no evidence of complement fixation, indicating a well focalized infection with no signs of activity.

While microscopic and cultural methods of demonstrating the fungus provide indisputable proof of coccidioidal infection, seldom is the diagnosis de-

pendent upon these lengthy and tedious laboratory procedures. Sputum studies are none too reliable because of the lack of adequate sputum in most patients and because of the difficulty in demonstrating the spherules by coverslip examinations. Further failure to recover the fungus does not rule out the possibility of infection. Animal inoculation following sputum culture on Sabouraud's medium will provide positive diagnostic proof of coccidioidal infection in doubtful cases. About ten to fourteen days after a heavy saline suspension of the culture is injected intra-peritoneally in a mouse, the animal usually dies, and spherule-containing lesions can be demonstrated in the mesentery, lungs, spleen, and other organs. The fungus also can be recovered in a guinea-pig following intra-testicular inoculation of sputum treated with 0.05% copper sulfate solution. Fortunately animal inoculations are rarely necessary to establish a definite diagnosis of coccidioidomycosis. Other simpler laboratory procedures will confirm the diagnosis more easily and with less work and danger for the laboratory personnel.

The Roentgen Diagnosis of Coccidioidomycosis.

Primary Coccidioidomycosis.

Some patients who present all of the clinical manifestations of primary coccidioidomycosis will show no recognizable roentgenographic changes. When present, however, the X-ray findings are restricted to the chest, and consist of the folowing changes, either alone or in combination:

1. Hilar thickening, consisting of soft, fuzzy, peri-bronchial infiltration in either hilar region, is the mildest change and usually clears within one to two weeks. There is nothing diagnostically specific about this manifestation; only by correlation with the clinical picture can differentiation be made from other fungus infections, non-specific tracheobronchitis, primary tuberculosis, or first stage silicosis. Hilar thickening is frequently associated with other chest findings, such as hilar or mediastinal lymphadenopathy, pneumonia-like infiltrations, or pleural fluid.

2. A pneumonia-like infiltration, the most frequent radiographic finding in primary coccidioidomycosis, is typically of a soft, hazy, homogeneous type, occurring either as an isolated patch or as an infiltration extending from the hilar region into the middle or lower lung field. Only in rare instances is the upper lung field involved and in these patients this pneumonia-like infiltration simulates the adult type of tuberculous infection. This form of coccidioidal involvement resembles certain primary a-typical pneumonias (virus pneumonitis, psittacosis, etc.), being more uniform, less blotchy, and more circumscribed than the usual bronchopneumonias, and only rarely suggests lobar distribution. In most patients this X-ray finding will persist for only a short time after subsidence of all clinical symptoms of active infection. Sometimes, however, the infiltration will be evident for many weeks or months after clinical recovery.

3. Nodular parenchymal lesions represent the most characteristic and diagnostically specific finding of primary coccidioidomycosis. This lesion is an isolated, well circumscribed nodular focus, averaging two to three centimeters in diameter, and occurring most frequently in the middle or lower lung field. In most patients these nodular lesions occur singly and are unaccompanied by other X-ray findings in the chest. They resemble

metastatic or embolic foci or uncalcified primary tuberculous nodules. If followed roentgenographically for periods of many months, this type of lesion is remarkably indolent, slow in evolution, and benign in character. Most of these lesions will develop central cavitation eventually. A coccidioidal cavity differs from other infectious excavations in the total lack of inflammatory change in the surrounding parenchyma. These cavities are thin walled and appear remarkably cyst-like, being sometimes mis-diagnosed as an infected congenital cyst. A coccidioidal cavity will disappear eventually, sometimes after many months, or shrink to a small residual fibrous nodule which may undergo calcification.

4. Mediastinal and hilar adenopathy is a relatively infrequent finding in primary coccidioidomycosis. When present, it is usually associated with parenchymal infiltration and a comparatively prolonged or severe clinical course. Occasionally, such adenopathy occurs alone and may be indistinguishable radiographically from Hodgkin's disease or other forms of mediastinal enlargement.

5. Pleural effusion is encountered in approximately one-fifth of all cases of primary coccidioidomycosis, usually in association with infiltration in the adjacent lung fields. The fluid is ordinarily unilateral and so limited in amount that it seldom more than obliterates the costophrenic angle. It resorbs rapidly and completely.

Progressive Coccidioidomycosis.

The great majority of primary coccidioidal infiltrations will disappear completely in five or six weeks so that continued spread of infiltration after this time is suggestive of the progressive form of the disease. Discovery of extra-pulmonary foci, particularly bone involvement, confirms the presence of progressive coccidioidomycosis and is of serious prognostic significance. The X-ray findings in progressive coccidioidal infections present the following characteristics, either alone or in combination:

1. Acute progressive pneumonic consolidations, which are especially prone to wide-spread dissemination, with death resulting within a few weeks or months.

2. Tuberculous-like infiltrations, localized at the apices or subapices, simulating the adult type of pulmonary tuberculosis in both location and character (clouding, mottling, fibrosis, and cavitation). Such a finding occasionally is seen in primary coccidioidomycosis when it resembles the exudative type of tuberculous infection.

3. Mediastinal adenopathy provides one of the most frequent and outstanding radiographic characteristics of progressive coccidioidomycosis. It is present in at least two-thirds of all cases in contrast to about one-sixth of all patients with primary coccidioidomycosis in which it is seldom so striking a feature as in the progressive type of the disease. When associated with primary coccidioidomycosis, it usually indicates a severe or prolonged infection.

4. Bone and joint involvement is frequent in the progressive form of the disease, occurring in approximately one-fourth of all patients. The lesions are typically cyst-like, sharply circumscribed areas of bone destruction, one-half to three centimeters in size with little change in the surrounding bone. Less commonly, a proliferative periostitis occurs, with or without accompanying destructive changes in the subjacent bone. These lesions are prone to localize in cancellous bone, particularly in bony ridges or prominences such as the tibial tubercle, malleoli, olecranon, styloid processes, acromion processes, and angles of the scapulae. They are also found in vertebral bodies, ribs, and the small bones of the hands and feet. Joints are involved by direct extension from subarticular foci, but only occasionally does primary synovial joint involvement occur. The latter type of arthritic lesion may closely simulate tuberculous arthritis. As in tuberculosis, the non-weight-bearing portions of the joints are primarily affected, and the joint cartilage is spared in the early stages of the disease.

5. Miliary dissemination is a frequent terminal manifestation of progressive coccidioidomycosis and is similar in its radiographic appearance to miliary tuberculosis, though the individual shadows tend to be less sharply defined and more fuzzy in outline than comparable lesions in tuberculosis. A high incidence of destructive bone foci accompanies the miliary phase of the disease. The appearance of small, punched-out areas of bone destruction at the margins of ribs, scapulae, or clavicles, in association with miliary involvement of the lungs, is nearly always pathognomonic of this form of progressive coccidioidal infection.

Prognosis.

No deaths have been reported as the result of primary coccidioidomycosis. Even with pulmonary cavitation the prognosis is excellent. On the other hand, the progressive form of the disease presents a grave outlook. After dissemination occurs, there is little chance of recovery. The course is sometimes rapid, terminating within four to six weeks, but in most instances the patient lives for many months, sometimes for a year or more. In rare instances the patient successfully focalizes his infection after an illness of long standing, and makes an eventual recovery.

Treatment.

In primary coccidioidomycosis the essential treatment is bed rest until complete clinical recovery is evidenced by: (1) the absence of physical findings; (2) a normal sedimentation rate; (3) a normal chest X-ray or at least roentgen evidence of regressing lung pathology; and (4) a low titer or a complete absence of precipitins and complement fixation in the patient's blood (if serologic tests are necessary). Even though many individuals in endemic areas have gone through an undiagnosed primary coccidioidal infection without difficulty, it is possible that some instances of progressive coccidioidomycosis could have been prevented by a strict rest regime in the early stages with the hope of arresting the infection and preventing dissemination. Isolation of the patient is not necessary, but the floors and walls of rooms and wards housing patients with progressive coccidioidomycosis should be lysolized daily to prevent growth of the fungus in cracks and crevices and to minimize dust formation.

Pulmonary cavitation requires no additional treatment, except pneumothorax or possible thoracic surgery in the rare patient with extensive pulmonary hemorrhage.

Patients with progressive coccidioidomycosis usually have been unaffected by the wide variety of drugs and vaccines which have been used in the past. These include sulfonamides, iodides, thymol, copper, antimony, and potassium tartrate intravenously, with x-ray therapy and various vaccine extracts of the fungus. Occasional "cures" have been reported, although most observers now attest to the hopelessness of the outcome in the majority of patients with the progressive form of the disease regardless of the treatment administered.

Military Considerations.

Coccidioidomycosis is of considerable importance to the Army Air Forces, especially the Western Flying Training Command, because of the location of a large number of training fields in the endemic areas. So far the mortality from progressive coccidioidomycosis has been exceedingly small, only seven deaths (all in negroes) having occurred in this command. Even though the mortality will continue to be low, due to the small number of disseminated infections, the morbidity of the primary form of the disease has been, and will continue to be, relatively high. Because of the advisability of rather prolonged hospitalization, even in patients with the milder form of the disease, the number of hospital days charged to coccidioidomycosis will always be considerable with a comparatively high non-effective rate resulting.

The increased susceptibility of negroes to both forms of coccidioidal infection makes it advisable to keep only essential colored troops on duty in endemic areas.

The recent observations indicating that desert rodents constitute a natural reservoir of coccidioidal infections in endemic areas offer a practical method of determining whether certain regions are safe for troop concentrations and maneuvers. The examination and culturing of the lungs from samples of rodents in various localities provide a dependable method of detecting whether Coccidioides is present in the environment. Alert Army doctors may very possibly discover new endemic areas during this global war.

From the viewpoint of the military surgeon, the important points in coccidioidomycosis are (1) recognition of the disease, and (2) prompt hospitalization of all clinical cases with continued bed rest until each patient's X-ray shows a progressive regression of the lung pathology, his sedimentation rate is normal, and until he is free from clinical signs of activity. With one-third of all American pilots and bombardiers receiving their cadet training in the Western Flying Training Command, it is possible that many of these men will acquire unrecognized coccidioidal infections during their training in endemic areas of the AAF/WFTC, and that weeks or months after completing their training, evidence of a still active infection may be discovered. Therefore Army

doctors everywhere, particularly flight surgeons assigned to tactical units, should be thoroughly familiar with all of the manifestations of this disease so that they will be able not only to diagnose acute and residual coccidioidal lesions, but to treat intelligently all military personnel with coccidioidal infections.

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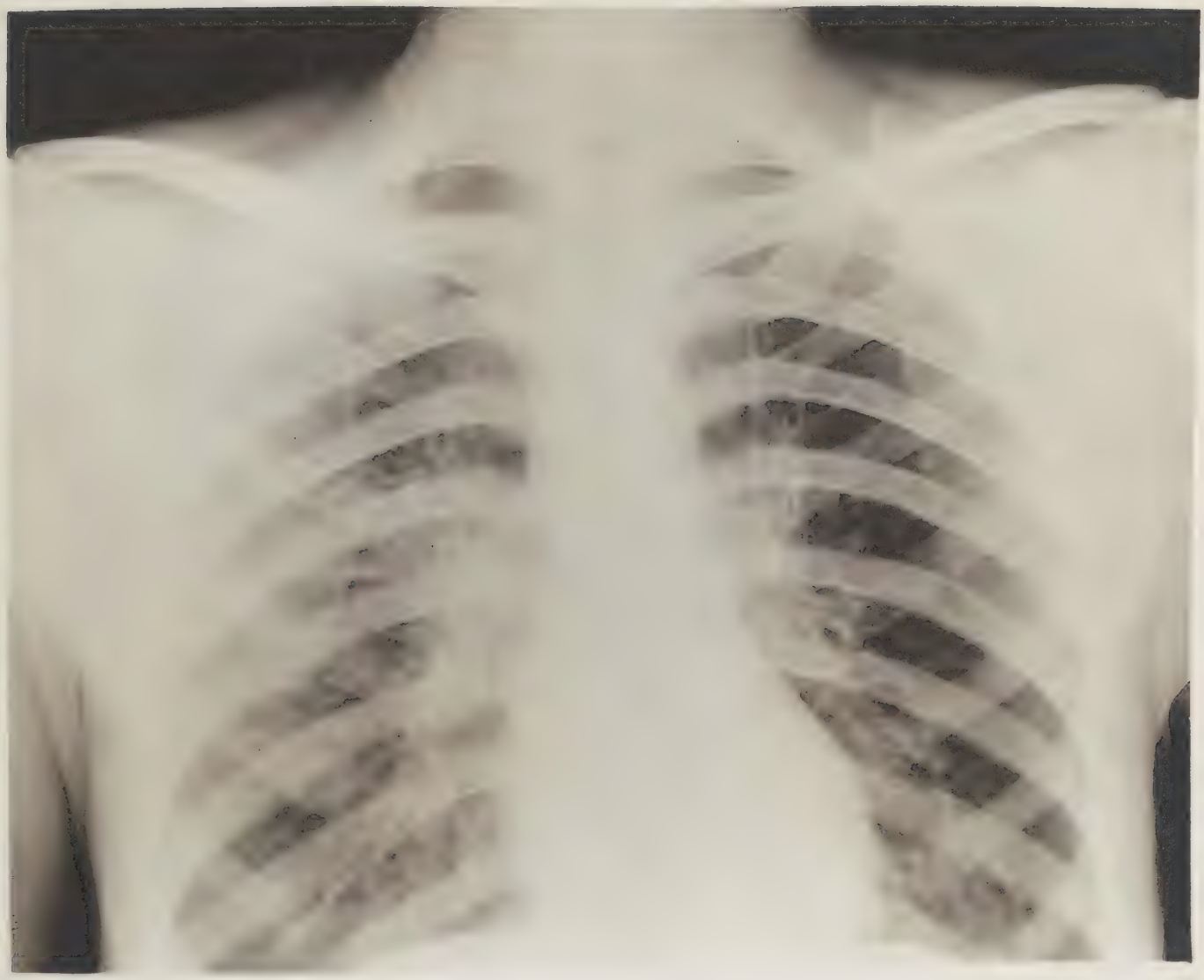


Fig. 1. Primary coccidioidomycosis.
Fuzzy peribronchial right hilar thickening.

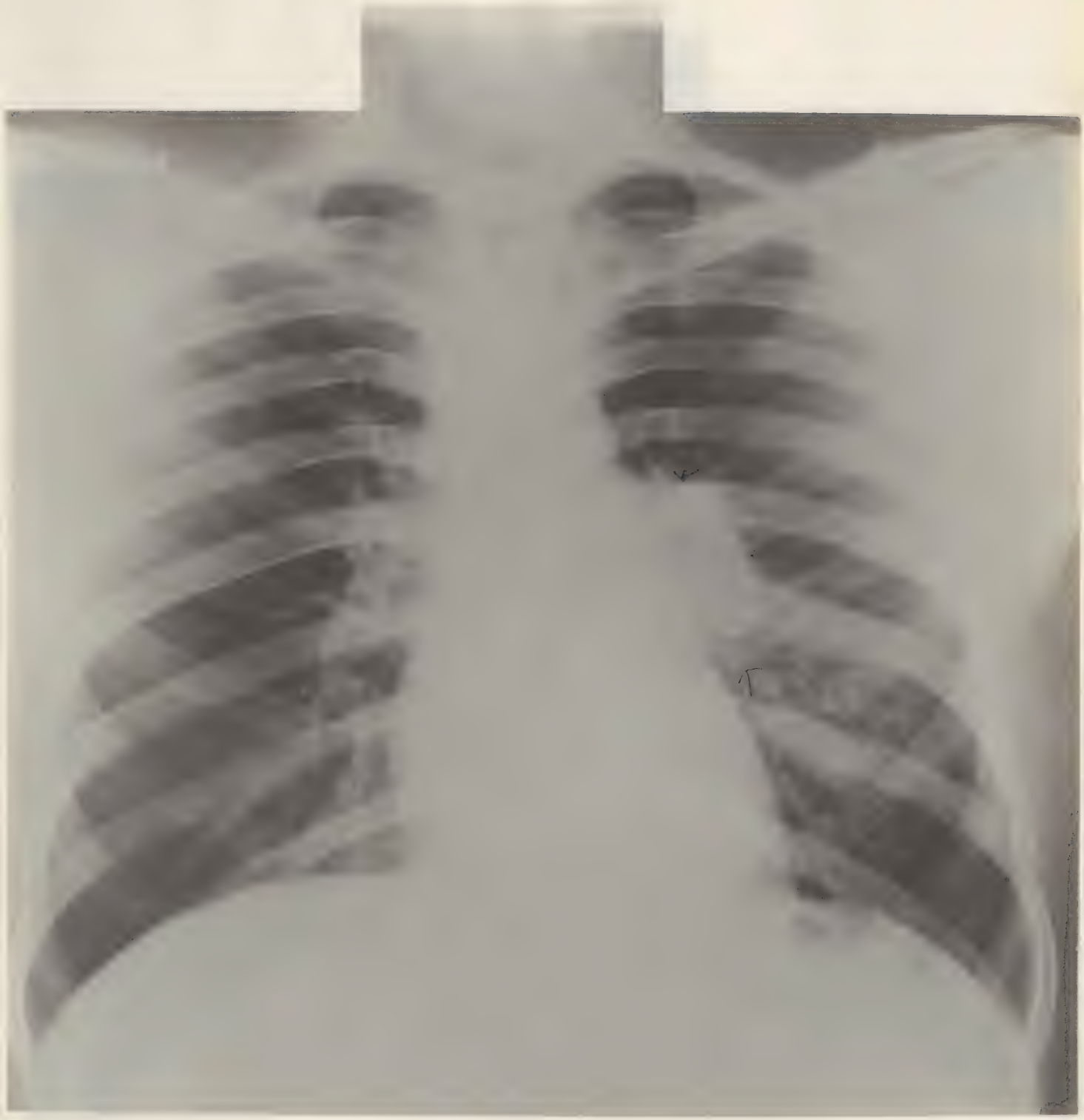


Fig. 2. Primary coccidioidomycosis.
Left hilar thickening. Slight prominence of right mediastinal border due to associated lymphadenopathy.

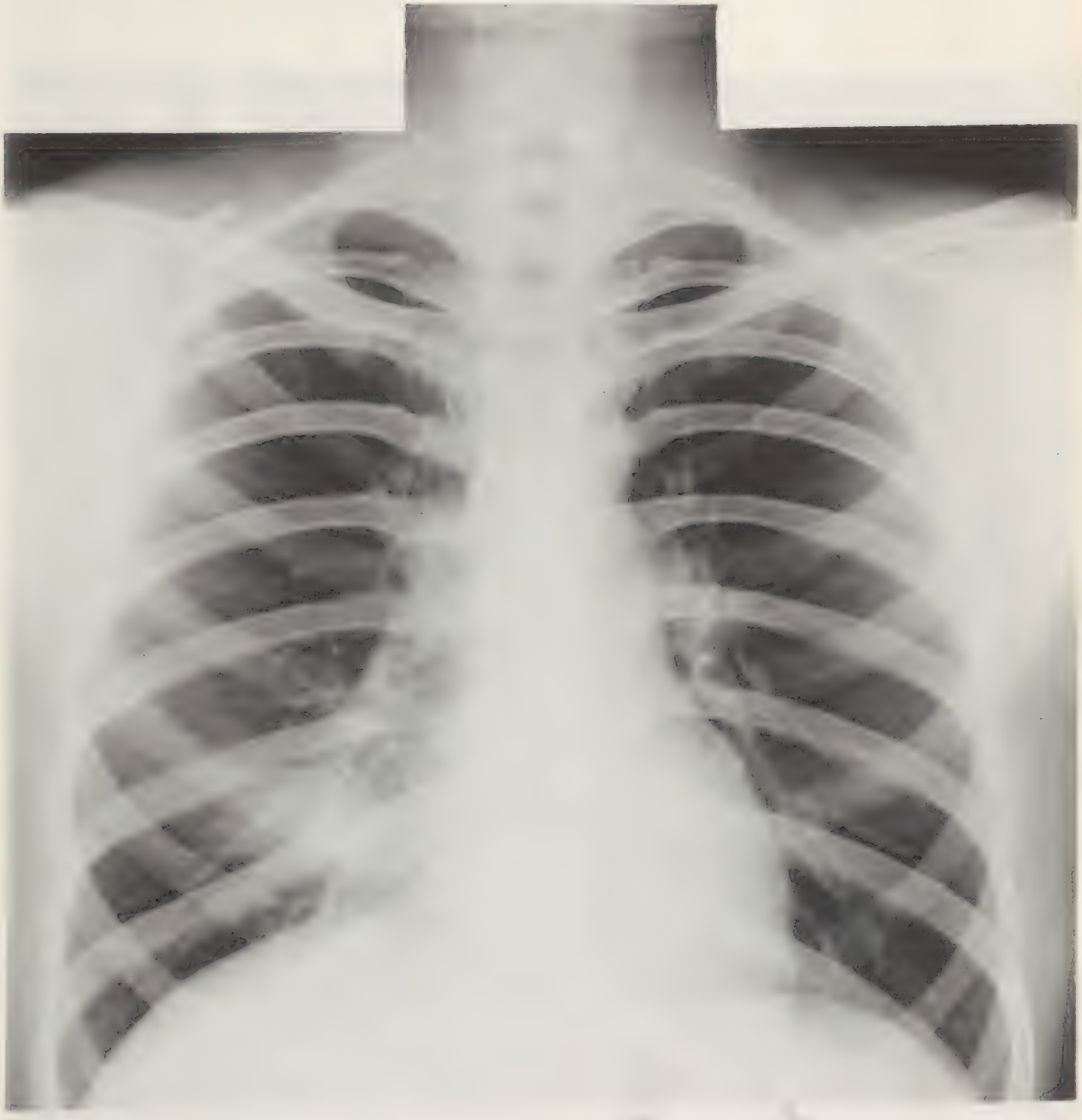


Fig. 3. Primary coccidioidomycosis.
Local zone of infiltration in the medio-basal portion of right lung.

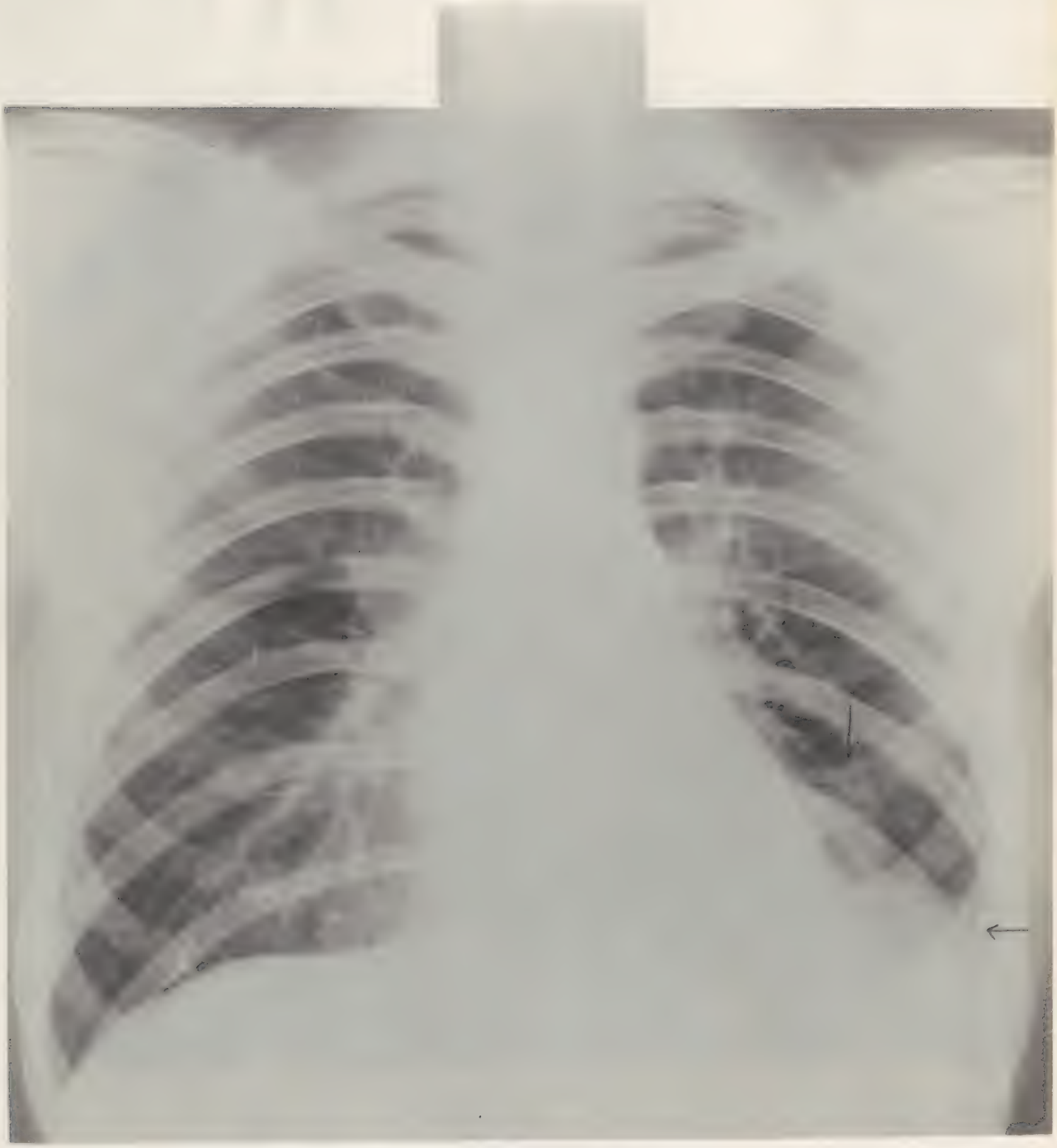


Fig. 4. Primary coccidioidomycosis.
Small amount of infiltration at the left base associated with slight pleural effusion.

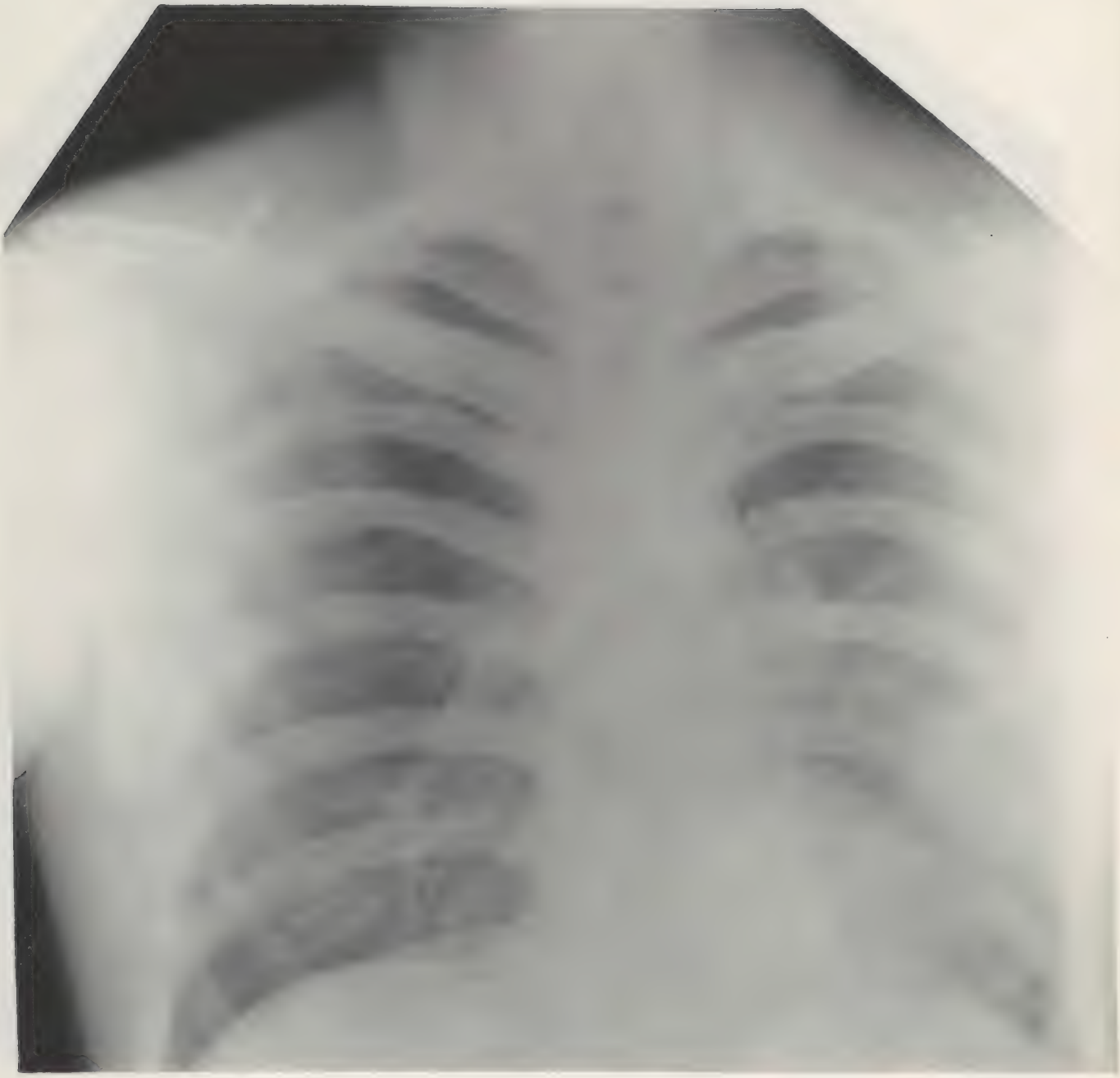


Fig. 5-A. Primary coccidioidomycosis.
Pneumonia-like infiltration in the left lower lung field.

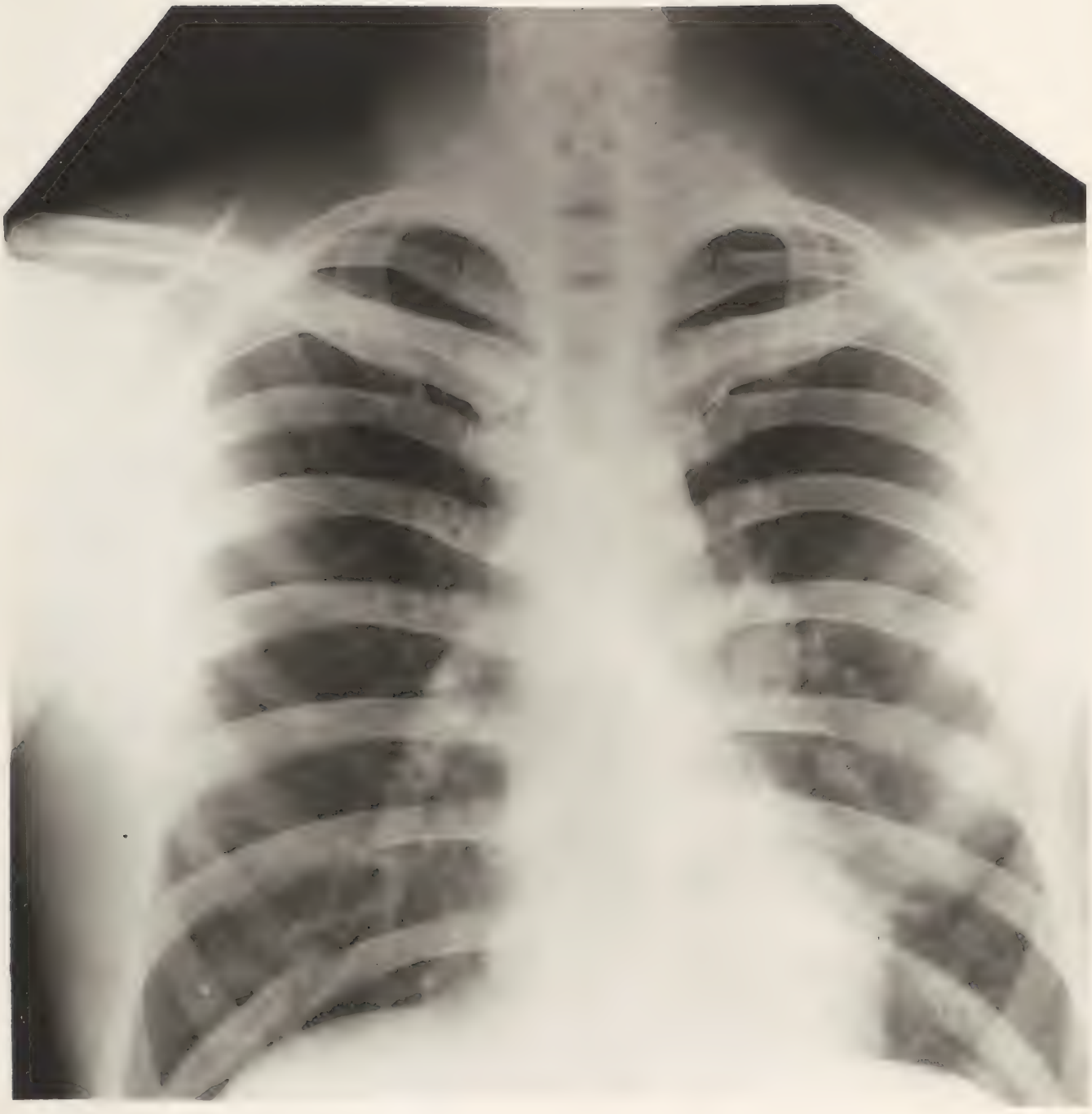


Fig. 5-B. Primary coccidioidomycosis.
The pneumonia-like infiltration shown in Fig. 5-A has largely but not entirely cleared after a period of three weeks.

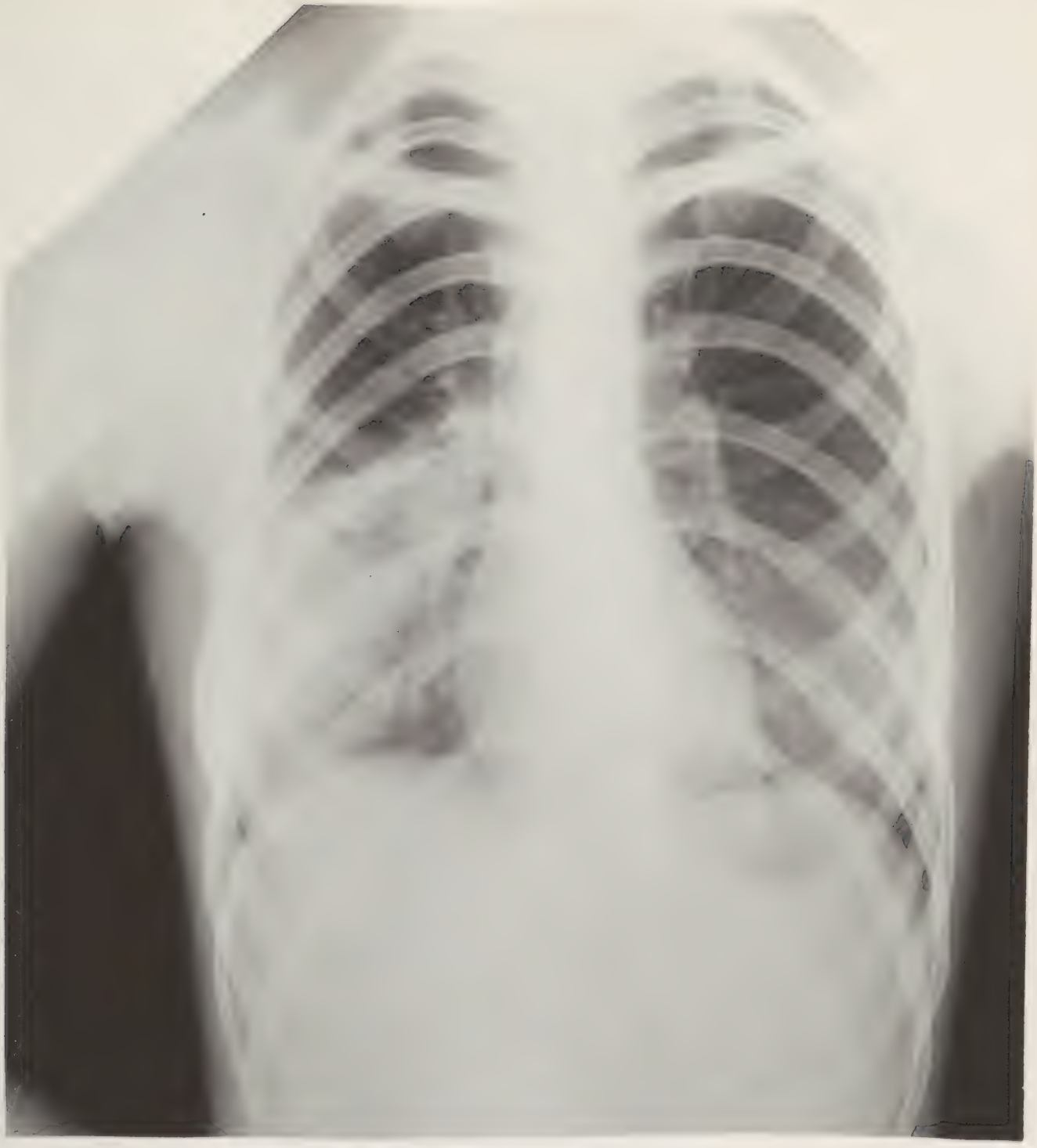


Fig. 6-A. Primary coccidioidomycosis.
Pneumonia-like infiltration in the right lower lung field.

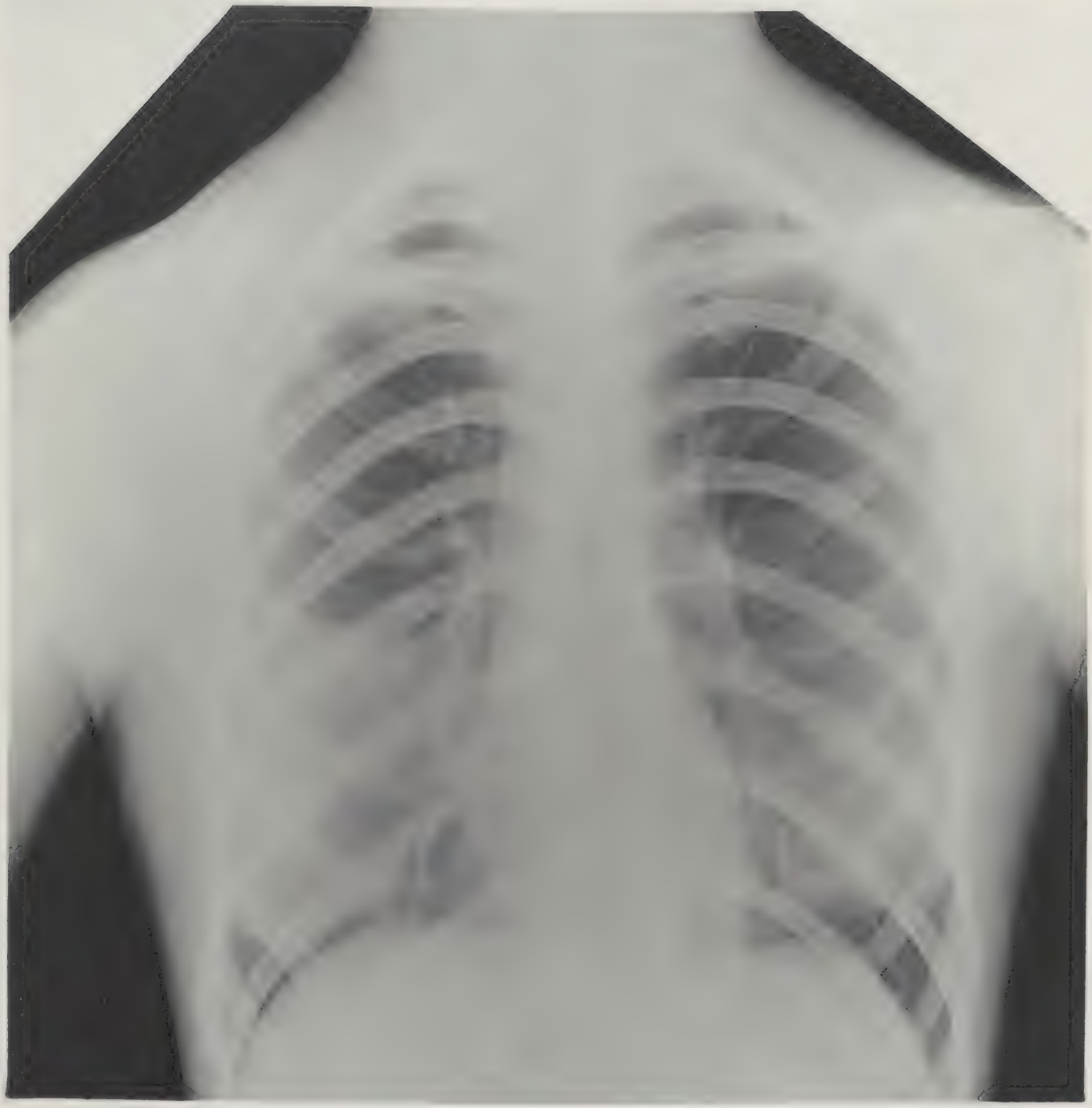


Fig. 6-B. Primary coccidioidomycosis.
The pneumonia-like infiltration shown in Fig. 6-A has largely cleared after an interval of one week.

Fig. 7-A. Primary coccidioidomycosis.
Severe illness. Massive hilar and mediastinal lymphadenopathy. Local zone of consolidation right lower lobe.

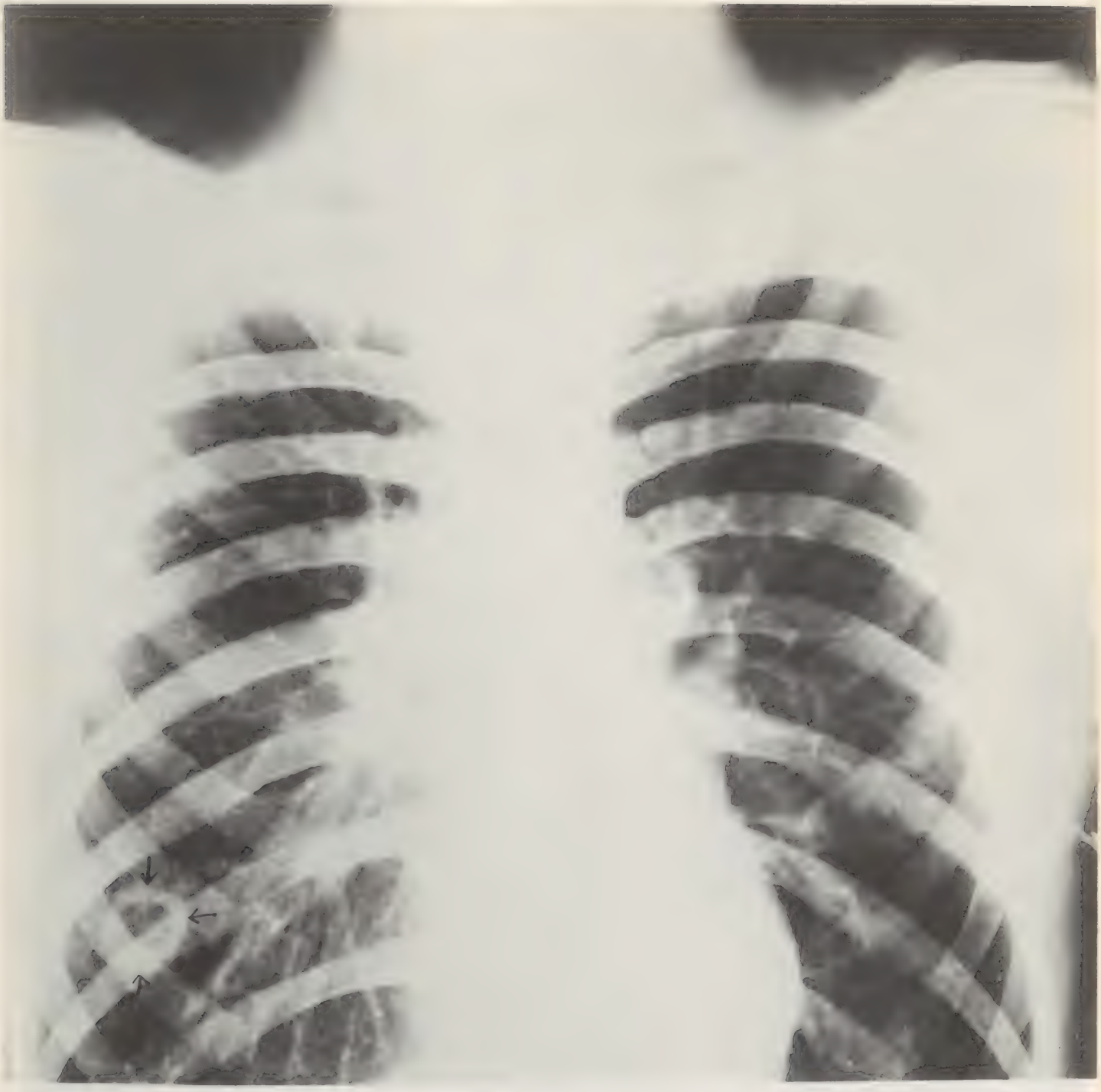


Fig. 7-B. Primary coccidioidomycosis.
The mediastinal and hilar lymphadenopathy shown in Fig. 7-A has regressed after a period of six weeks; the local zone of infiltration at the right base has been replaced by an isolated ring-like cavity.

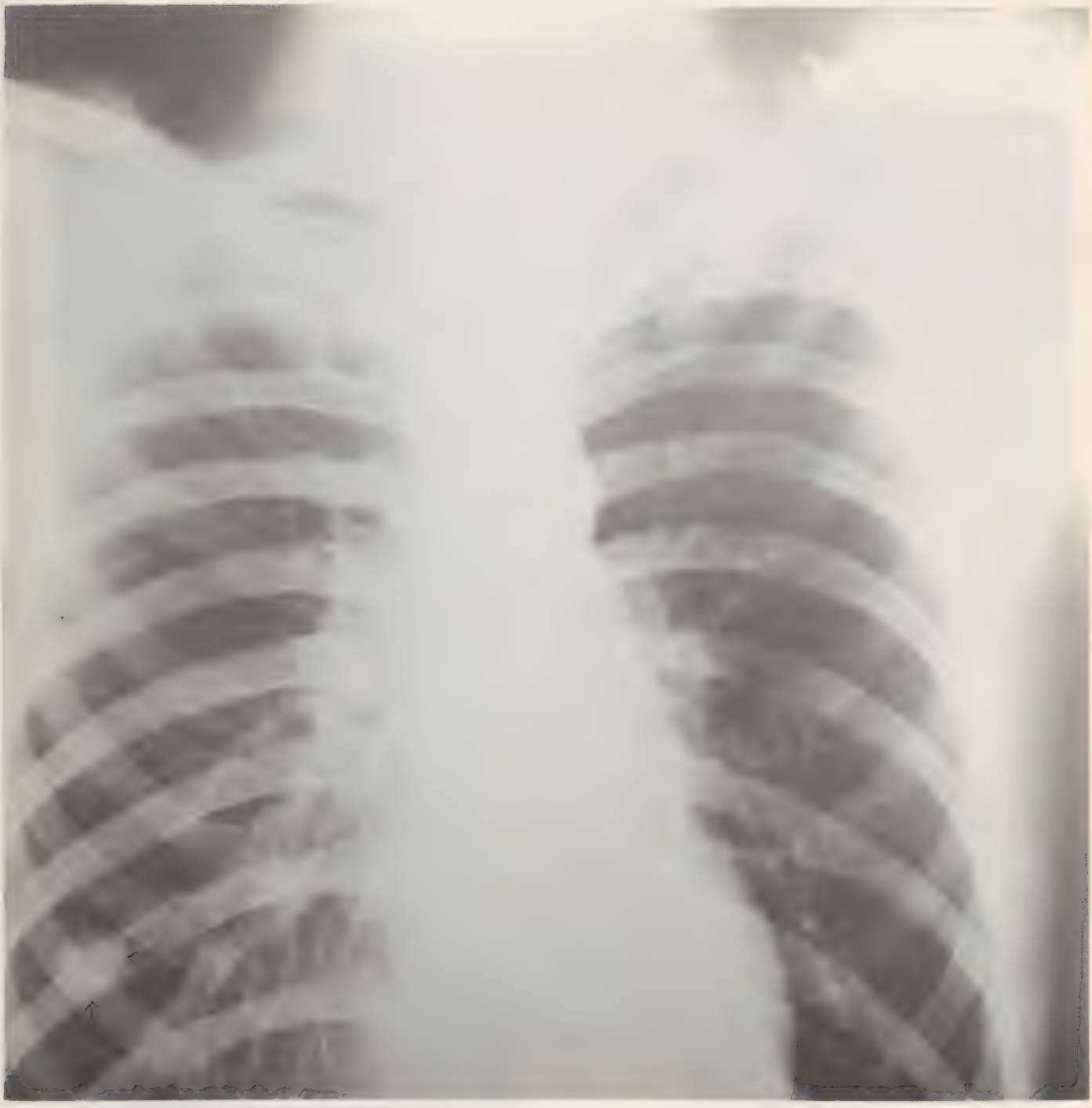


Fig. 7-C. Primary coccidioidomycosis.
The mediastinal and hilar lymphadenopathy shown in Fig. 7-B has further regressed after a period of ten weeks; the cavity previously present has disappeared leaving a residual nodule.

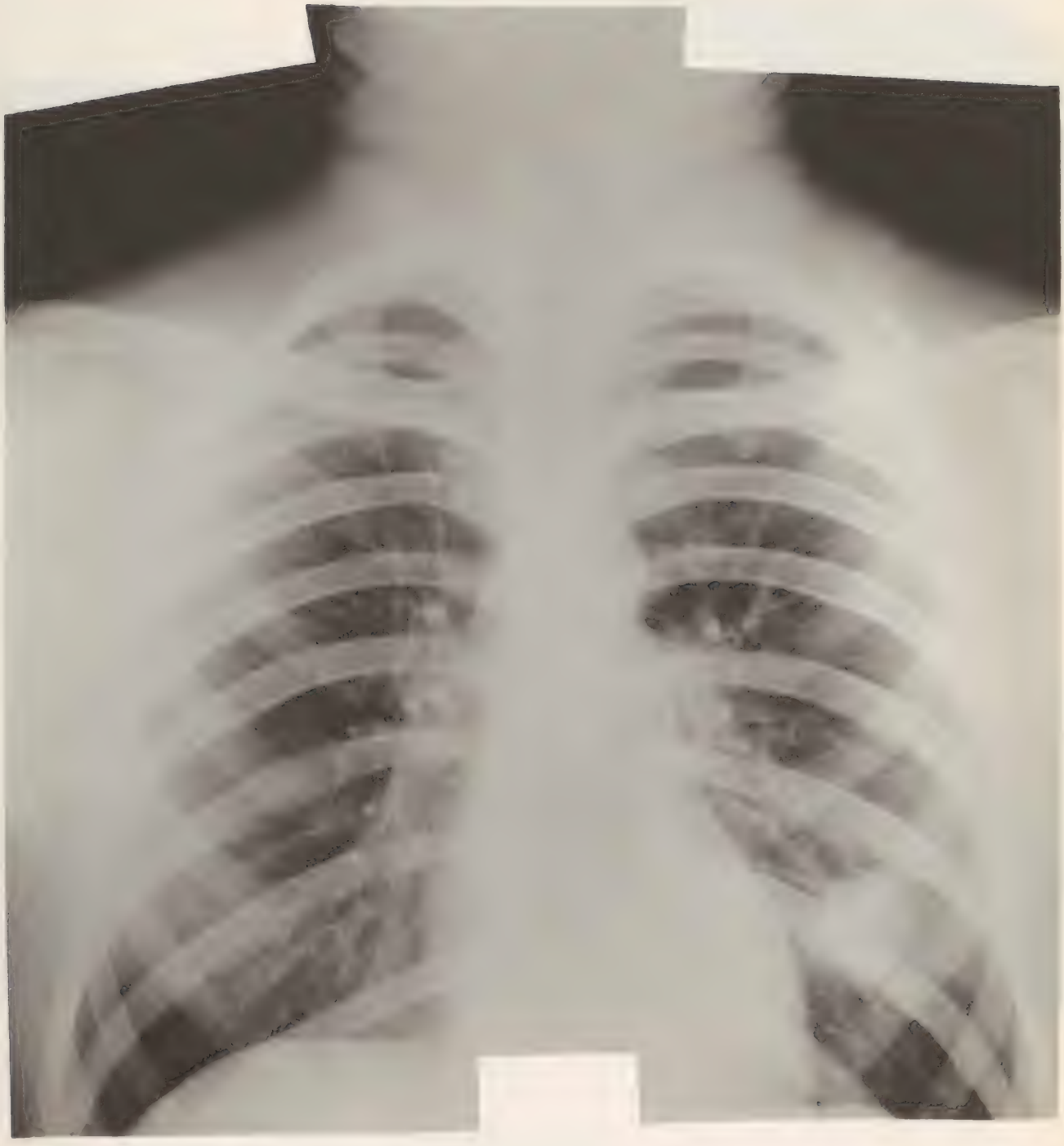


Fig. 8-A. Primary coccidioidomycosis.
Nodular, well circumscribed lesion in the lower left lung field.

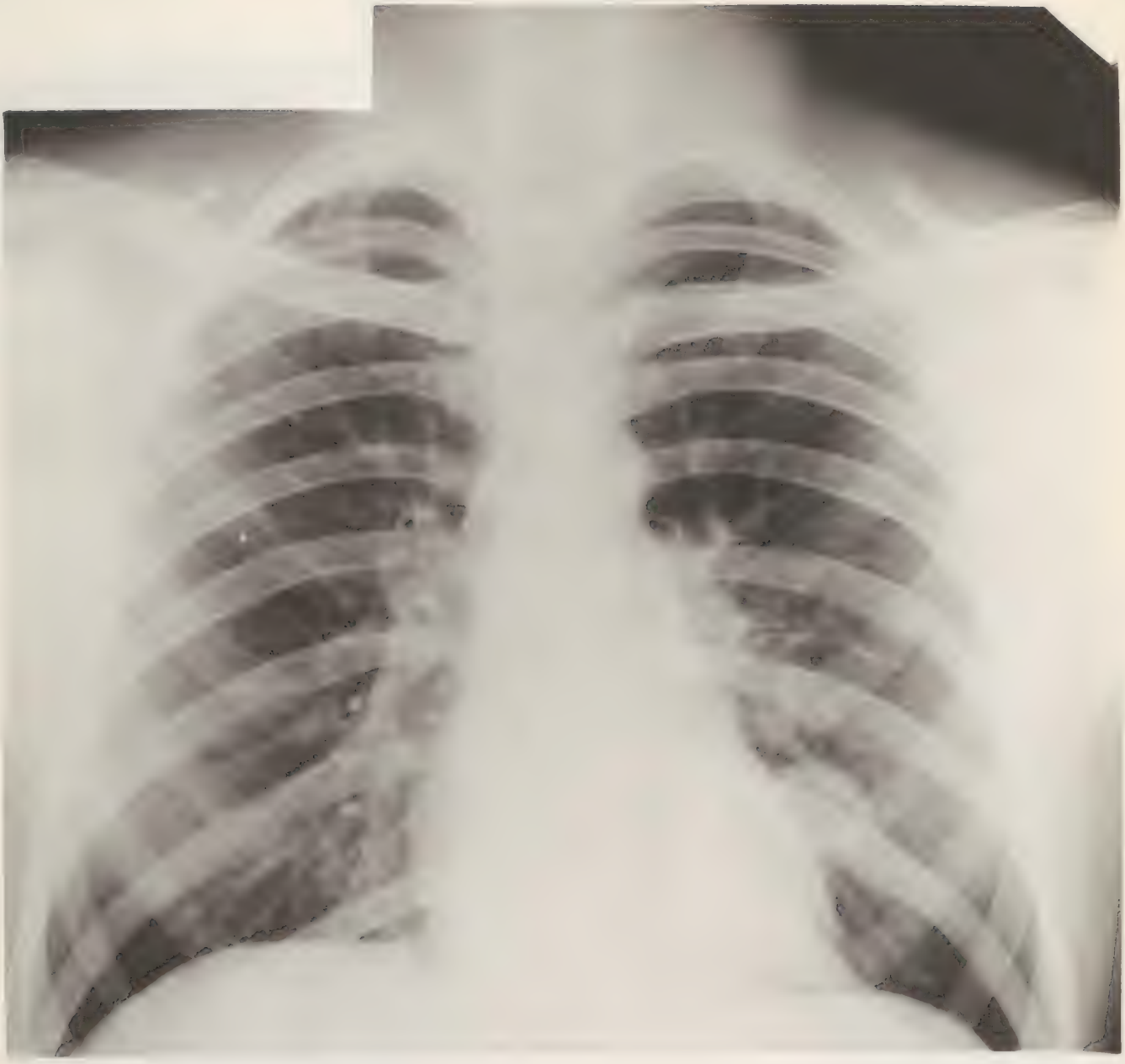


Fig. 8-B. Primary coccidioidomycosis.
The nodular lesion in the left lower lung field shown in Fig. 8-A is developing central cavitation after a period of six months.

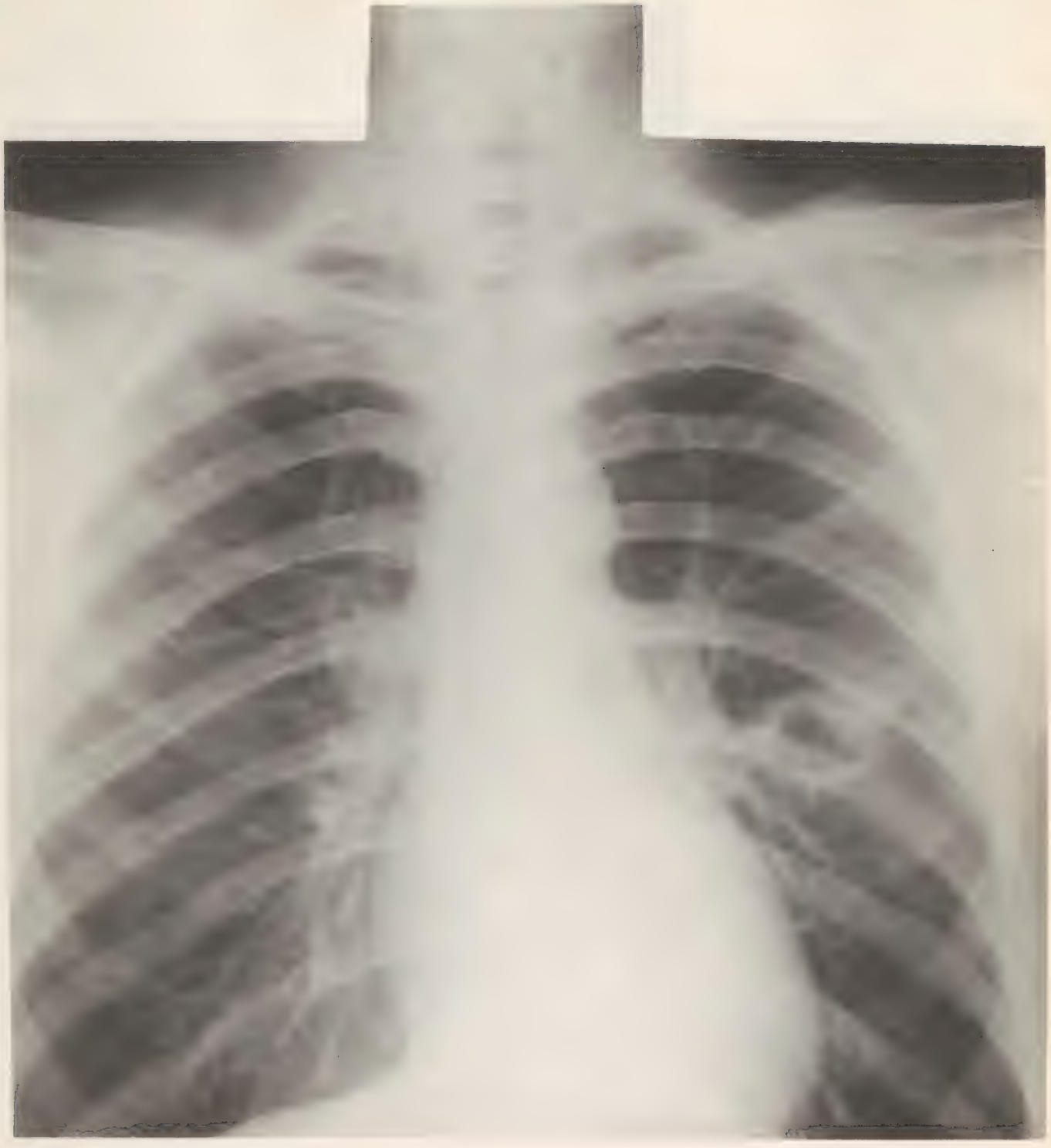


Fig. 9. Primary coccidioidomycosis.
Typical ring-like cavity in the left mid-lung field.

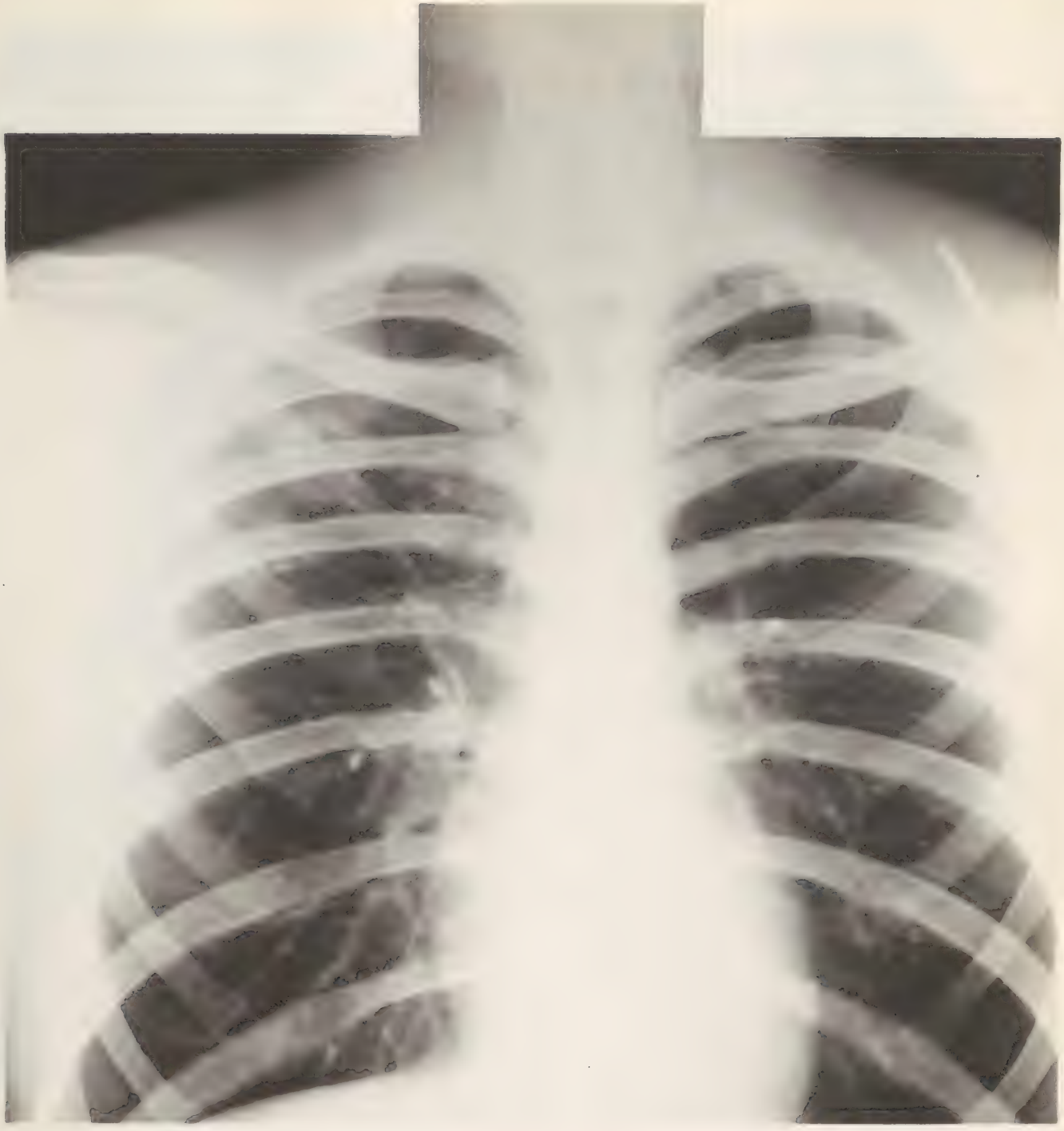


Fig. 10. Primary coccidioidomycosis.
Ring-like cavity in the right subclavicular region simulating tuberculosis. The wall of the cavity became pencil thin after a three months' interval, resembling that of a congenital cyst. The outlines of this cyst-like lesion then gradually "melted away" after a six months' interval.

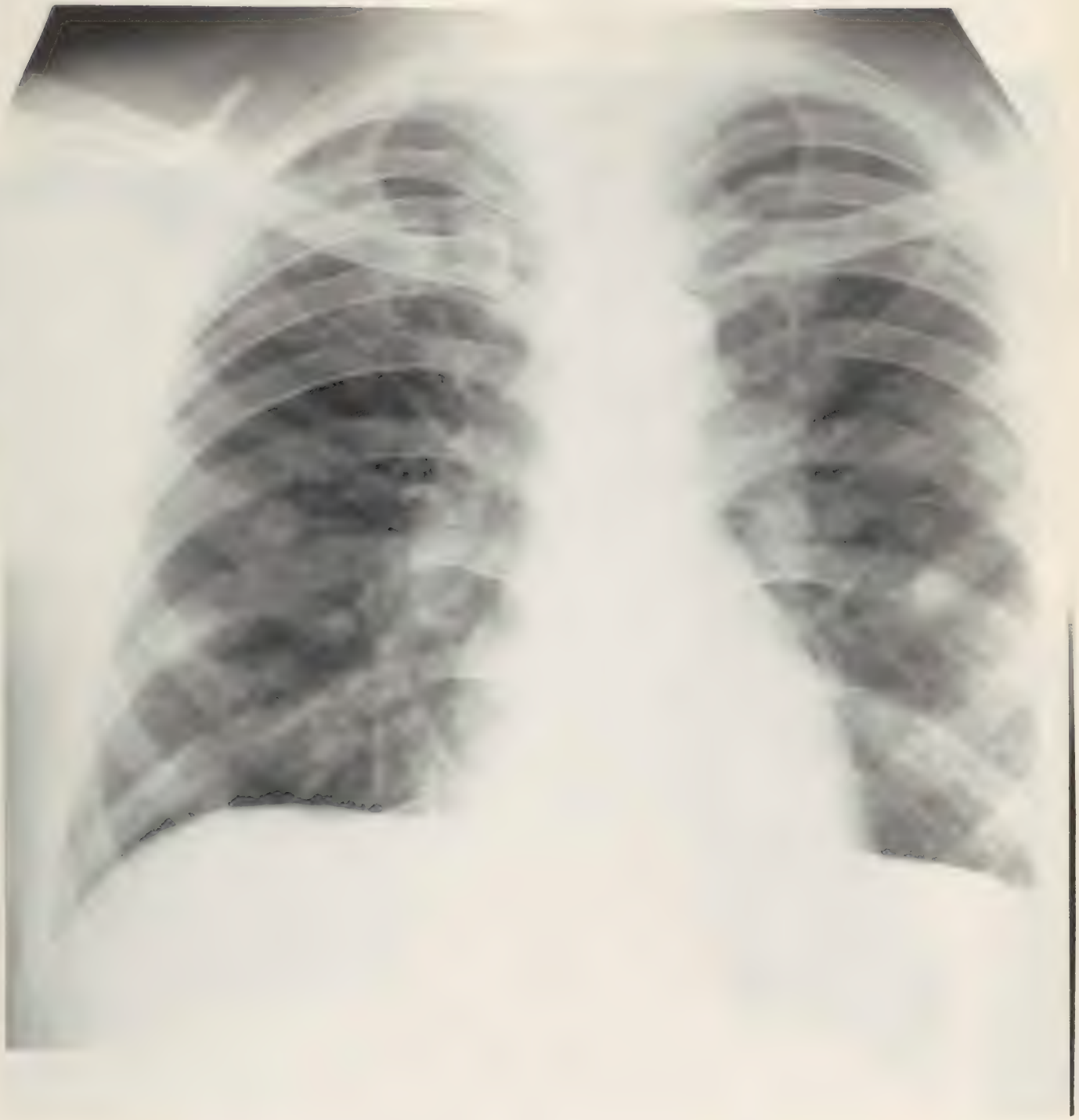


Fig. 11. Primary coccidioidomycosis.
An unusual case showing multiple nodular foci simulating metastatic carcinoma or multiple septic emboli. Central cavitation is visible in some of the nodules. This patient has shown progressive improvement both clinically and radiographically without evidence of extra thoracic dissemination.

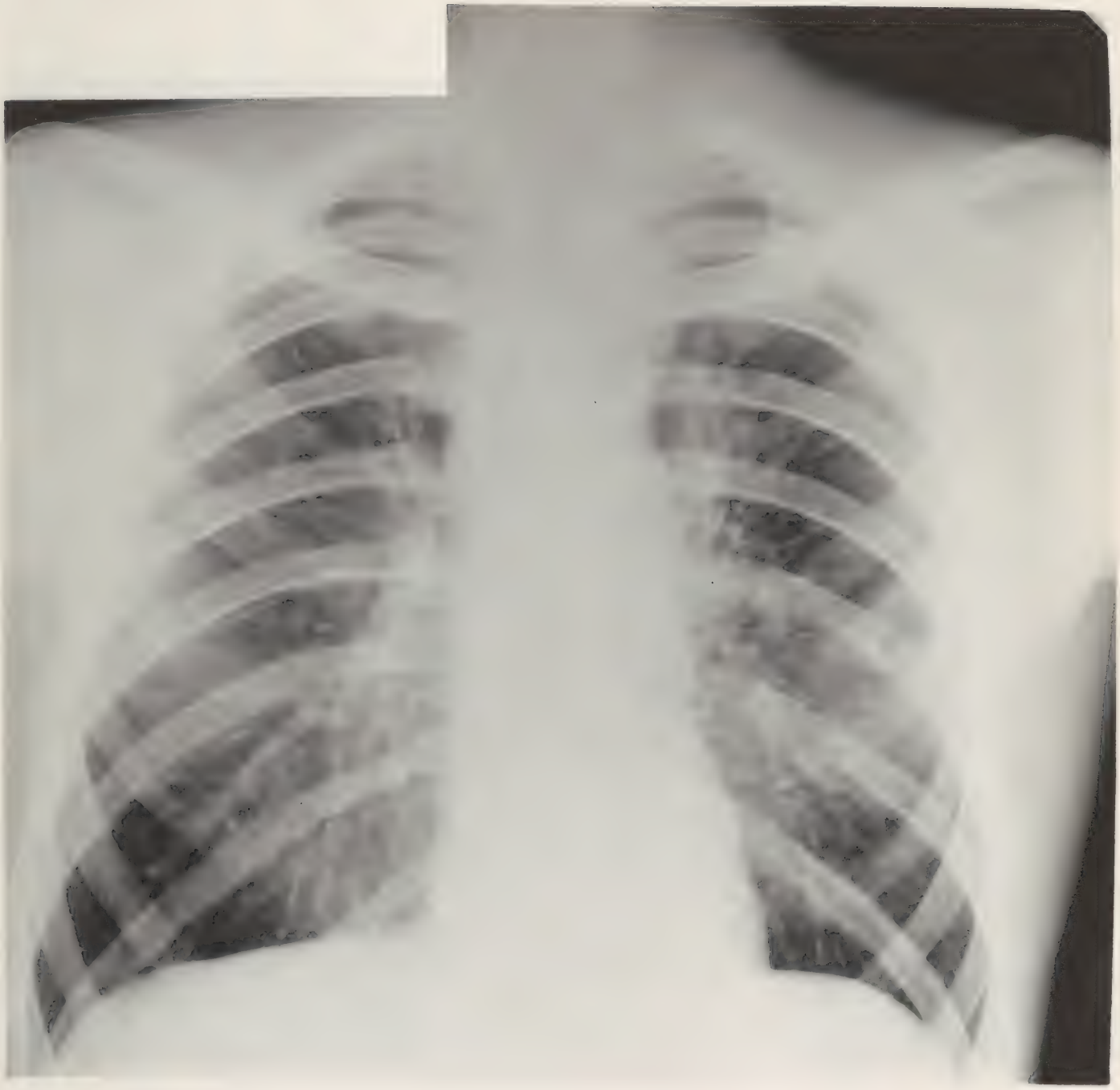


Fig. 12. Primary coccidioidomycosis.
Lumpy mediastinal broadening. Infiltration radiating from the hilar regions. (Chest films entirely normal after a period of two and one-half months).

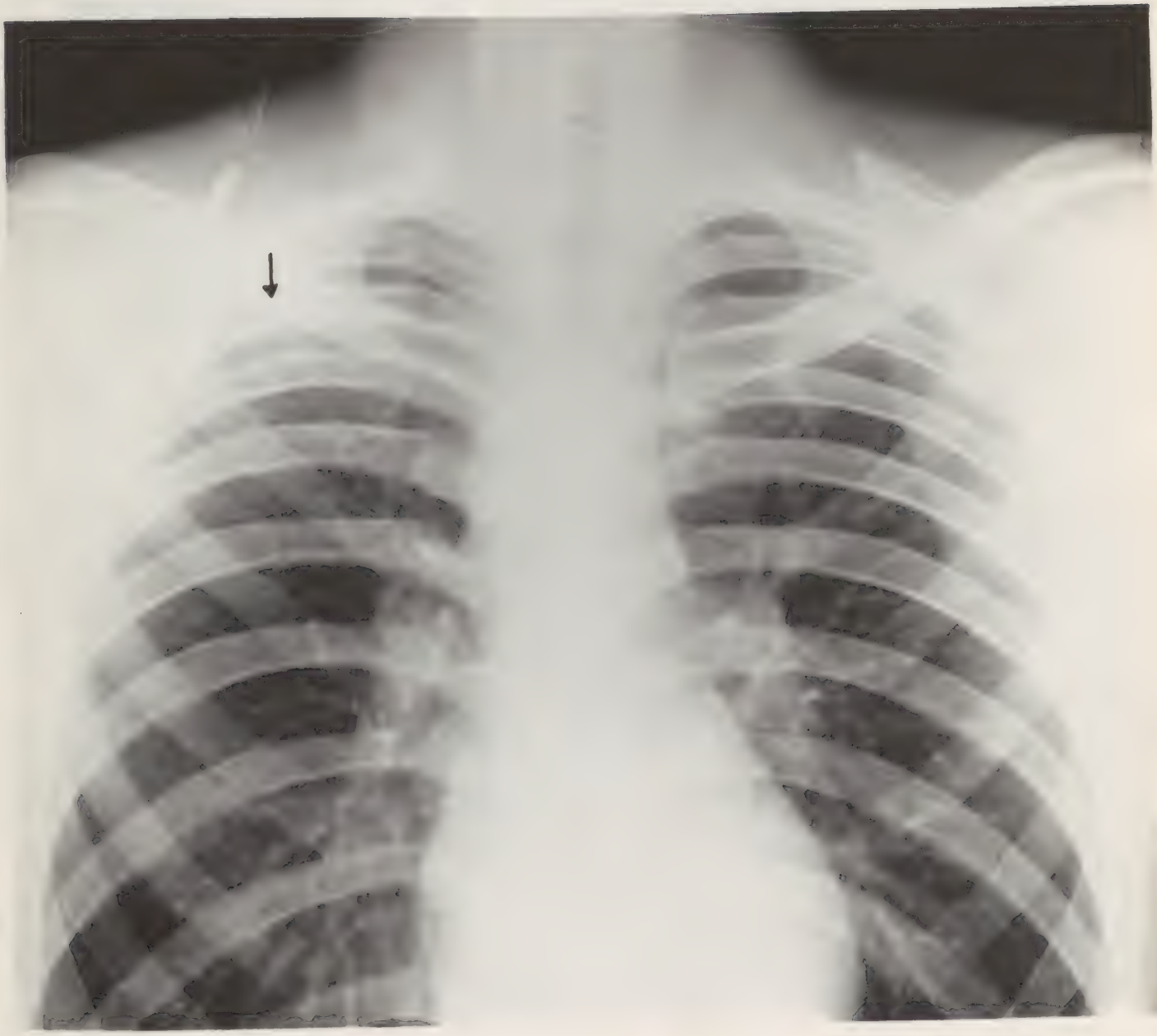


Fig. 13. Secondary coccidioidomycosis (coccidioidal granuloma). A local zone of soft exudative infiltration is seen in the right first interspace. Note the lumpy, widened right mediastinal border due to associated mediastinal lymphadenopathy.

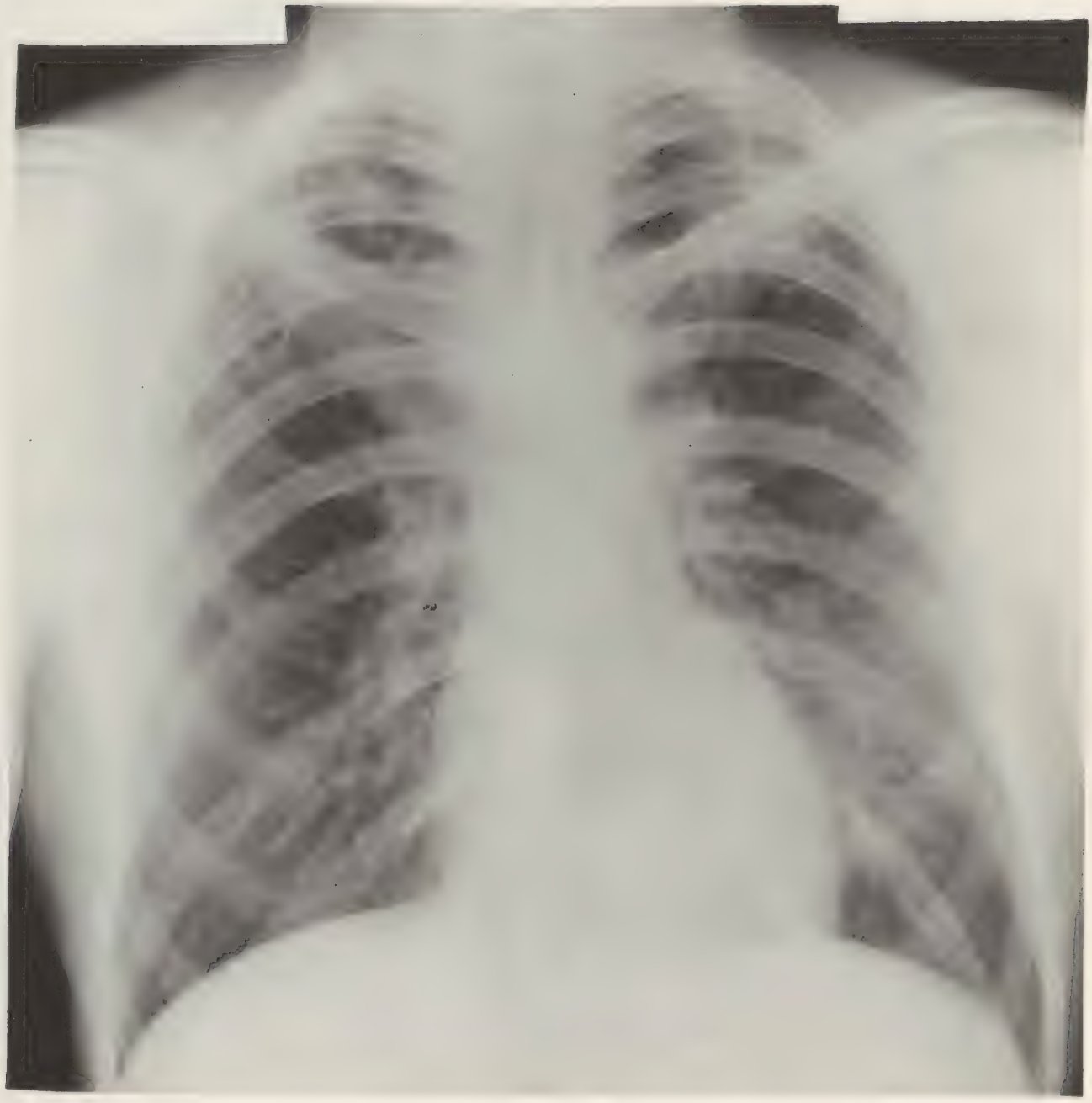


Fig. 14. Secondary coccidioidomycosis (coccidioidal granuloma).
Tuberculosis-like patchy and strand-like infiltration at both apices and sub-apices.
Note the thin wall cavities just below the clavicles on each side.

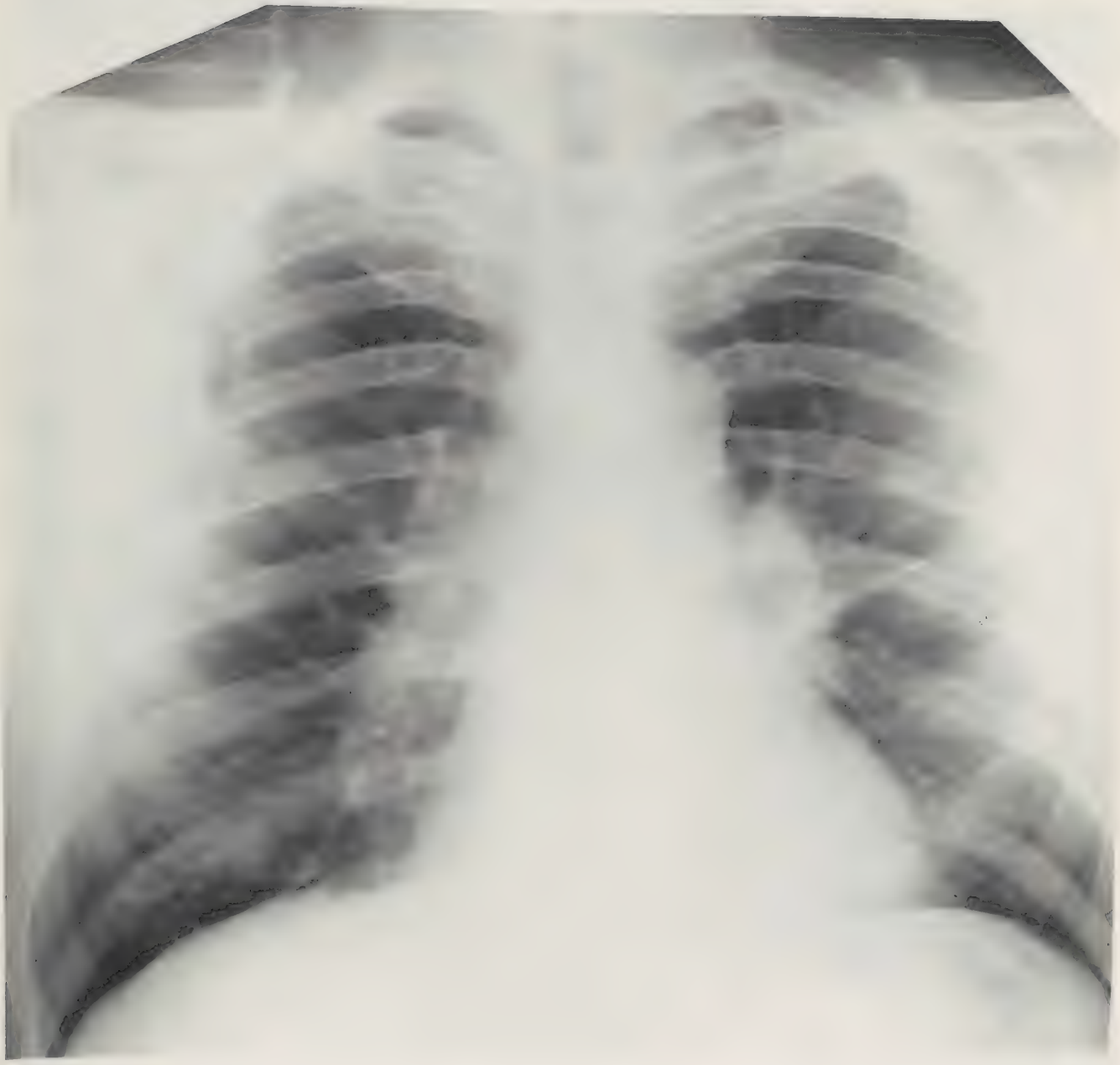


Fig. 15. Secondary coccidioidomycosis (coccidioidal granuloma). Hilar and mediastinal lymphadenopathy.

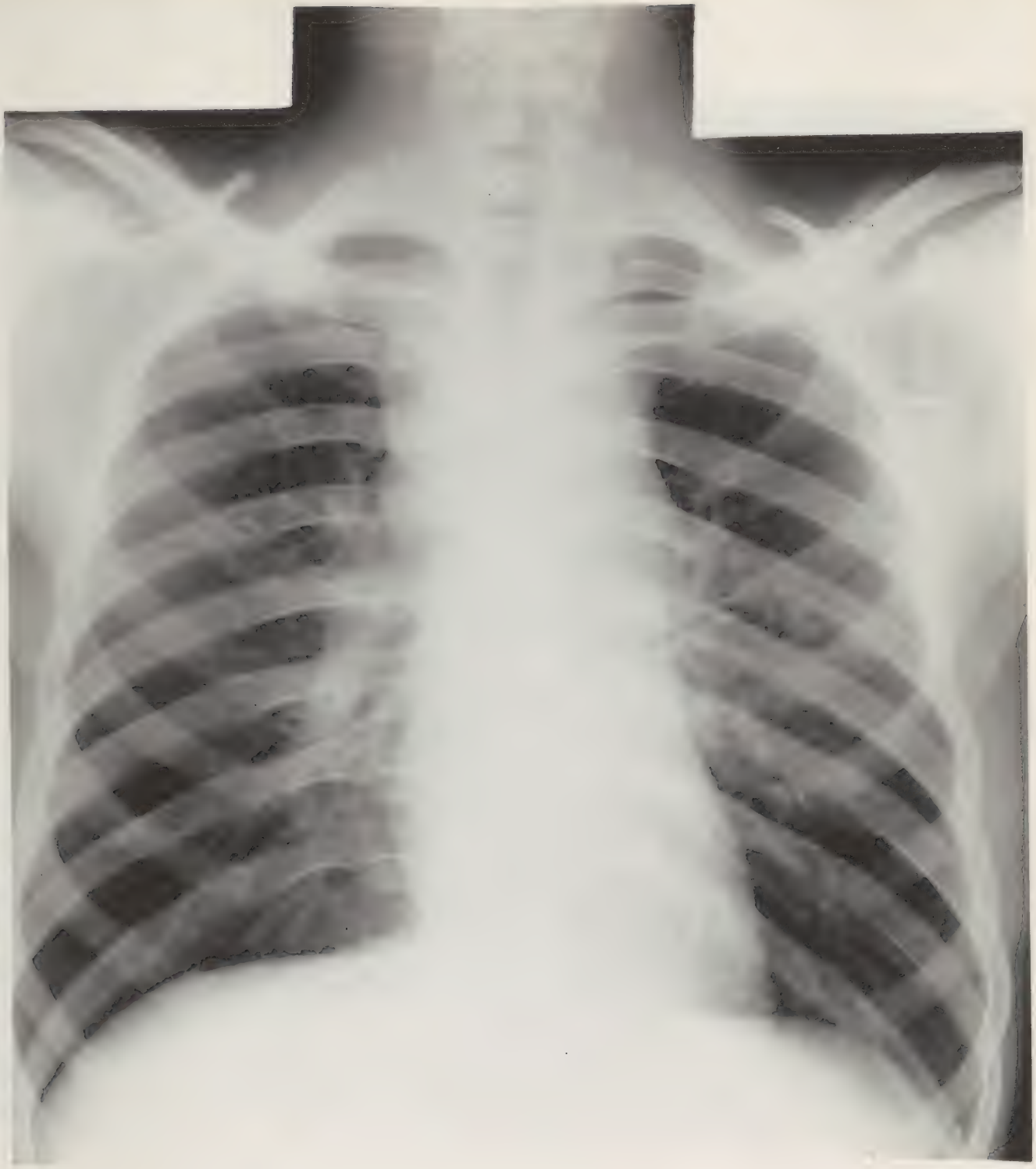


Fig. 16. Secondary coccidioidomycosis (coccidioidal granuloma). Massive mediastinal lymphadenopathy simulating lymphoblastoma. General dissemination with fatal termination four months after onset.

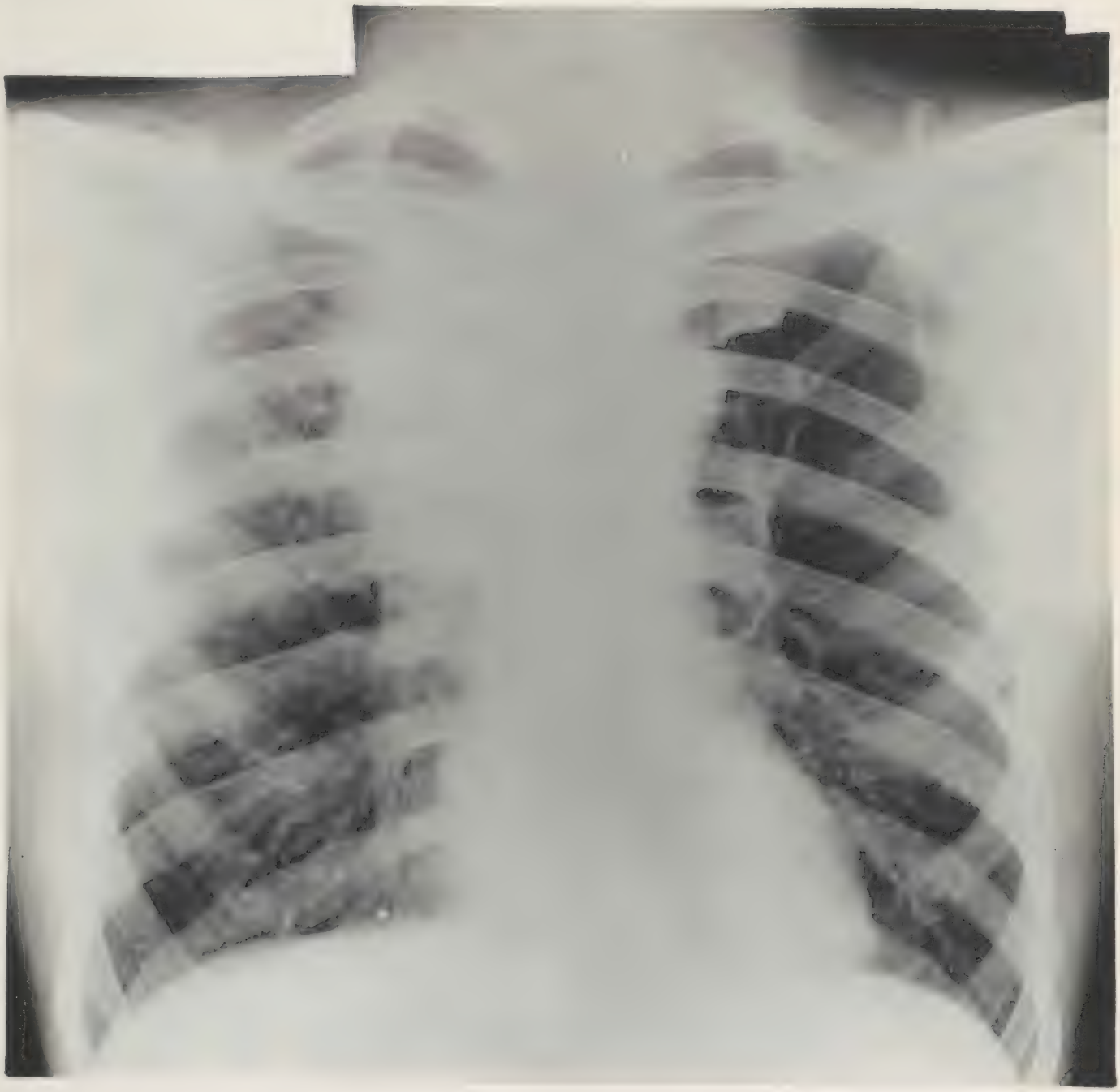


Fig. 17. Secondary coccidioidomycosis (coccidioidal granuloma). Dense shadow projecting from the right mediastinal border consisting of mediastinal lymphadenopathy and associated parenchymal infiltration. Terminal miliary dissemination.

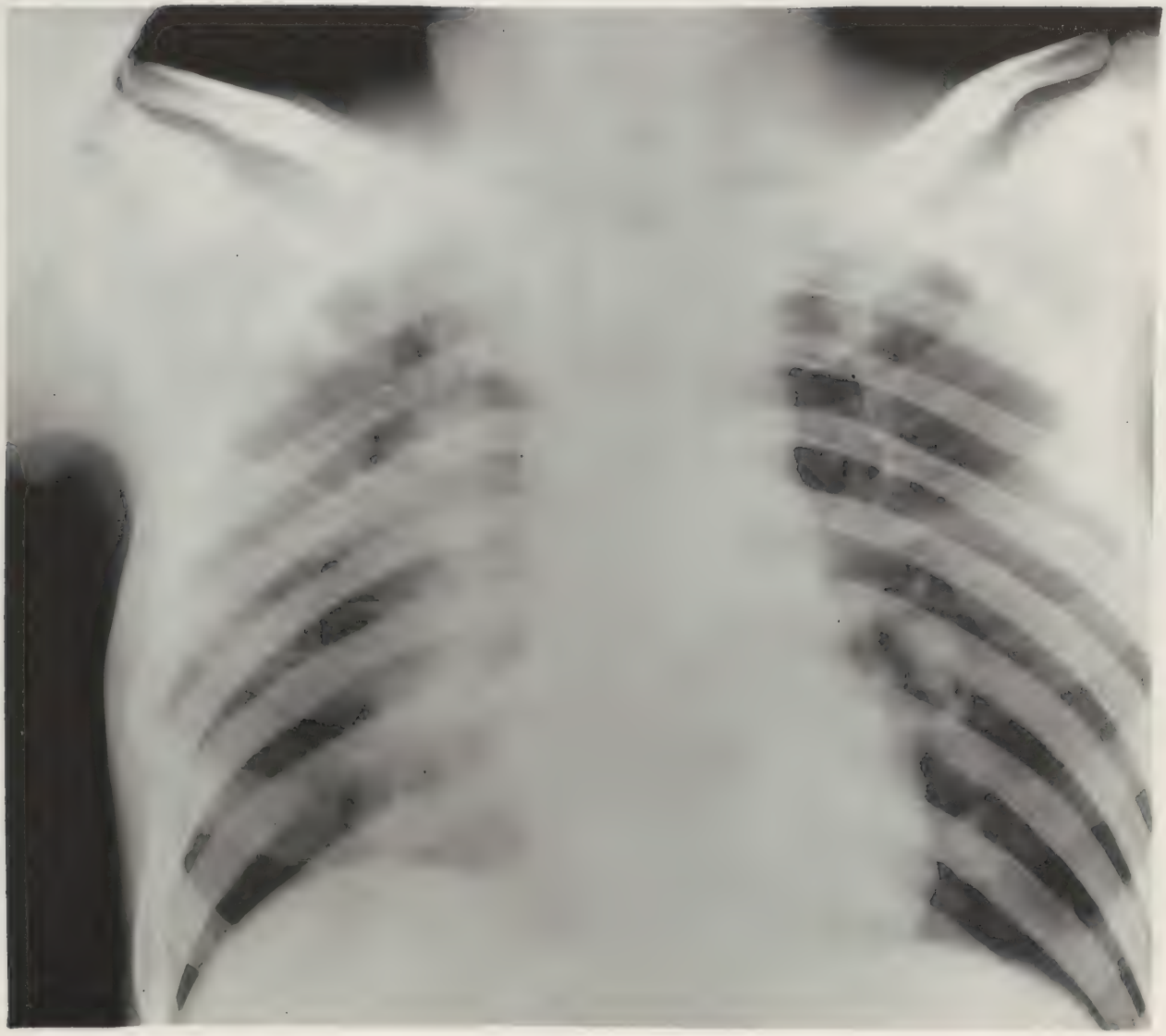


Fig. 18. Secondary coccidioidomycosis (coccidioidal granuloma). Diffuse pneumonia-like infiltration radiating from the right hilum. Broad mediastinum due to associated lymphadenopathy.

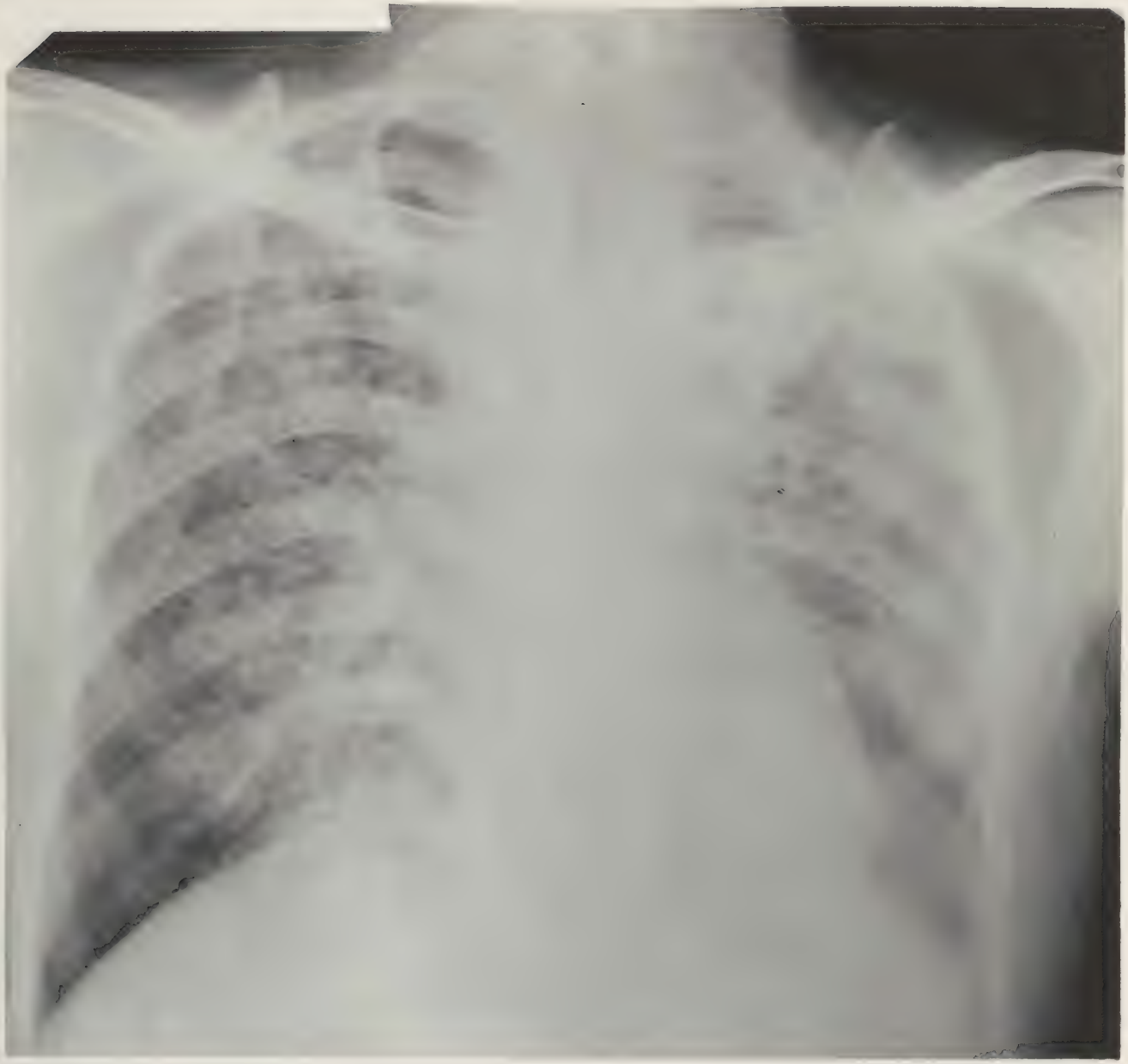


Fig. 19. Secondary coccidioidomycosis. (coccidioidal granuloma). Extensive diffuse nodular infiltration throughout both lungs. Confluent zone of consolidation at the left apex. Mediastinal lymphadenopathy.

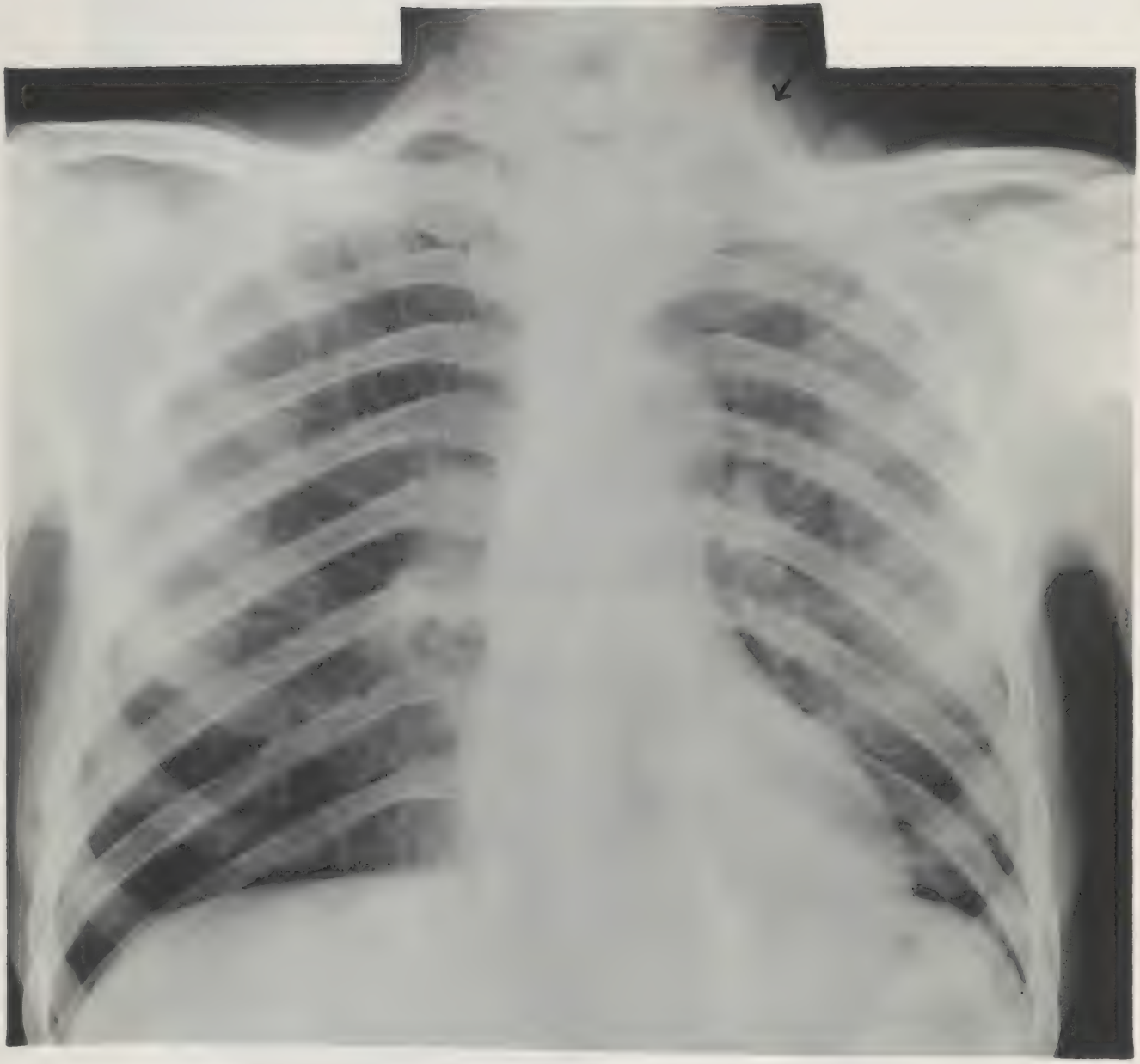


Fig. 20. Secondary coccidioidomycosis (coccidioidal granuloma). Miliary spread. Note area of bone destruction in tubercle of left first rib.

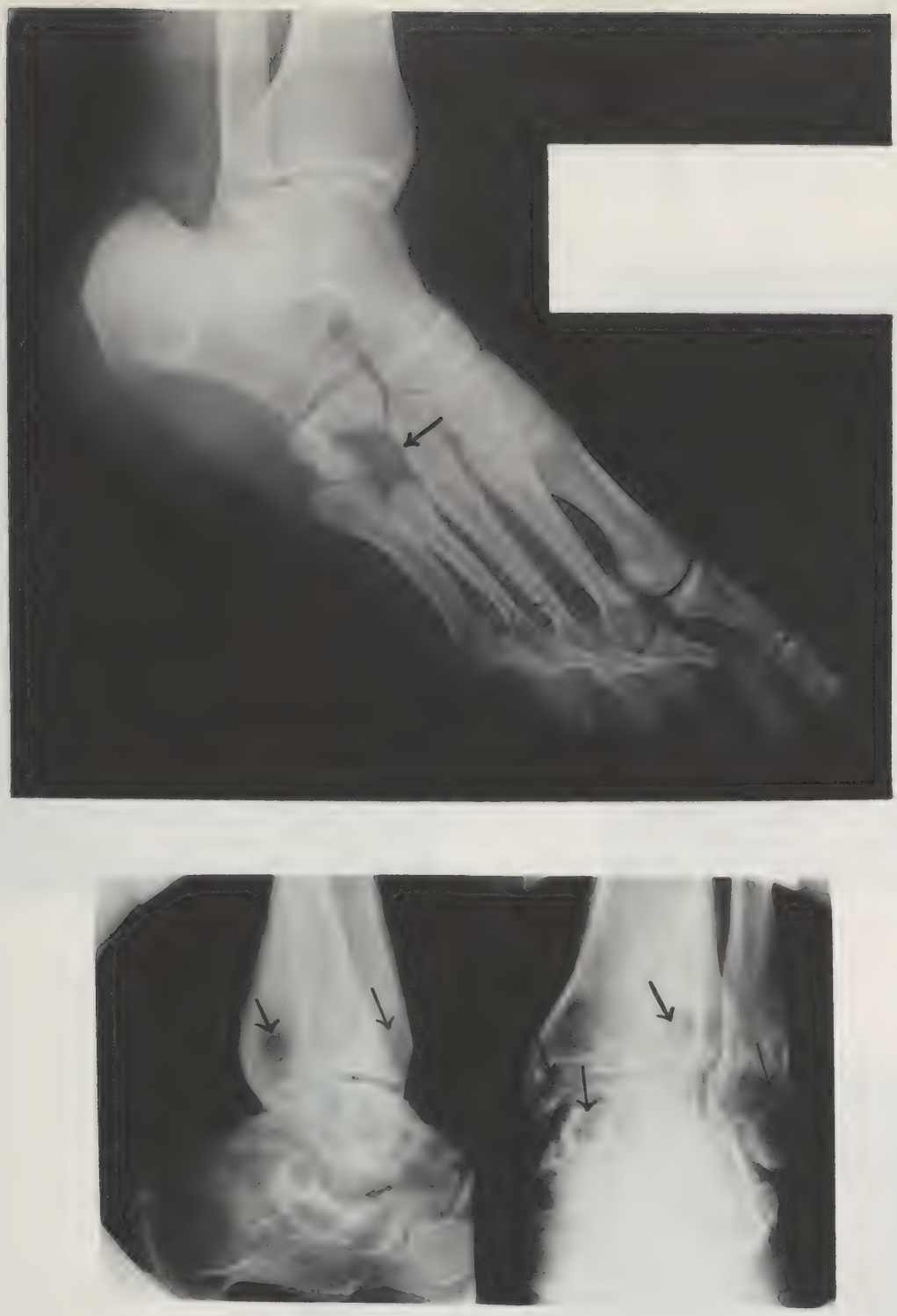
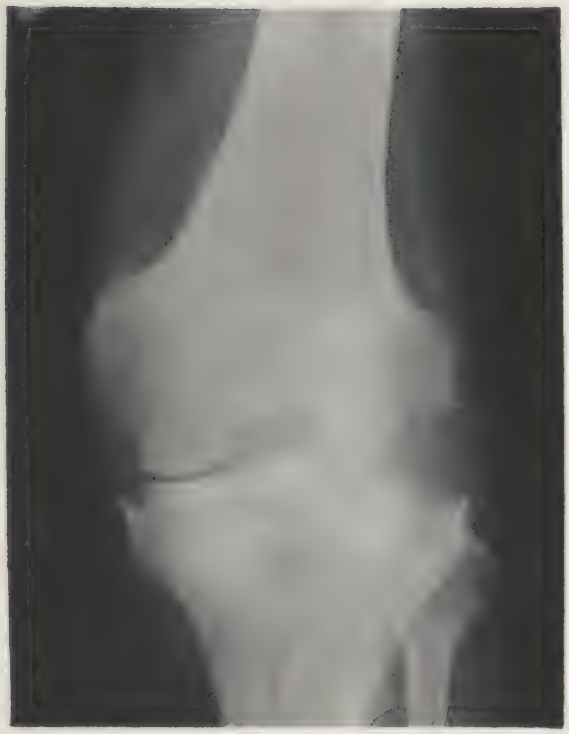
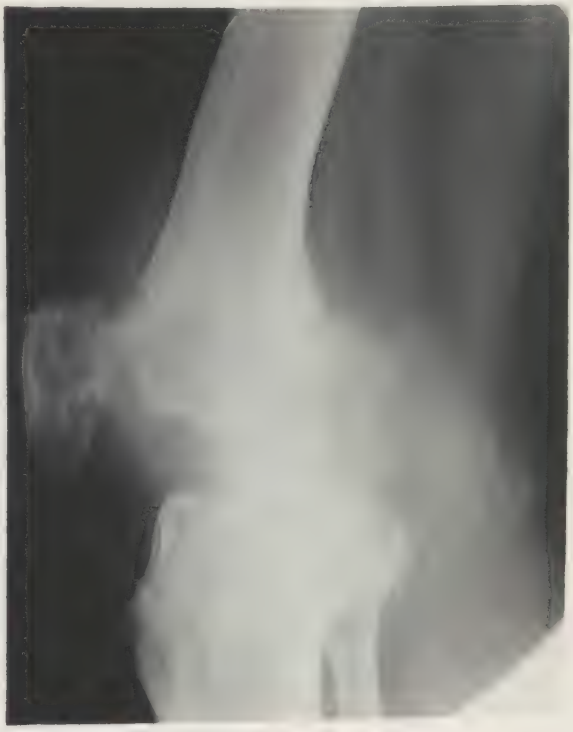


Fig. 21. Secondary coccidioidomycosis (coccidioidal granuloma).
(Upper) - Destruction of a portion of the cuboid bone.
(Lower) - Cyst-like areas of destruction in the distal tibia, malleoli and talus.

Fig. 22. Secondary coccidioidomycosis (coccidioidal granuloma).
(Upper) - Destructive arthritis involving non-weight bearing portions of joint.
(Lower) - Proliferative periostitis at anterior surface of patella.





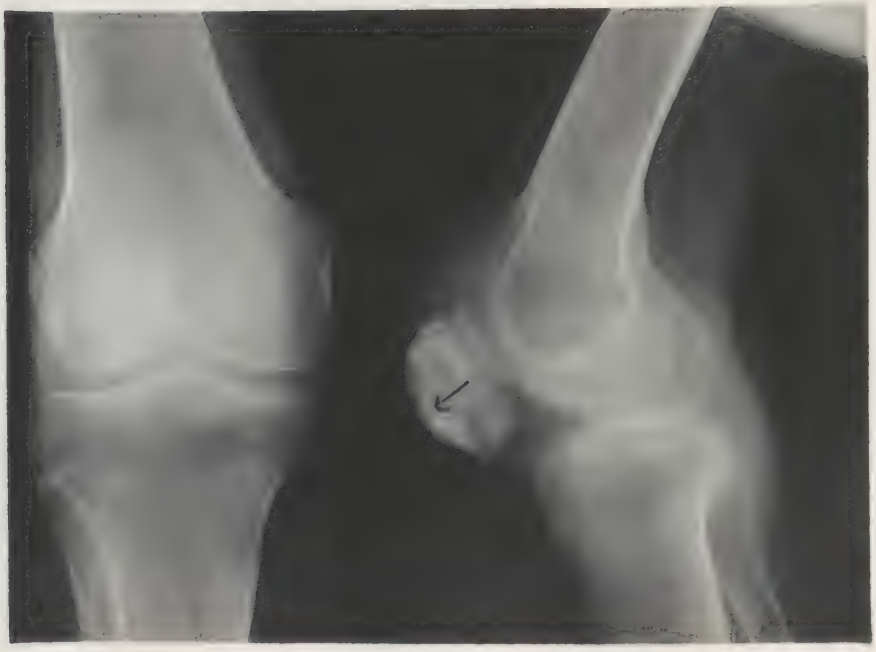
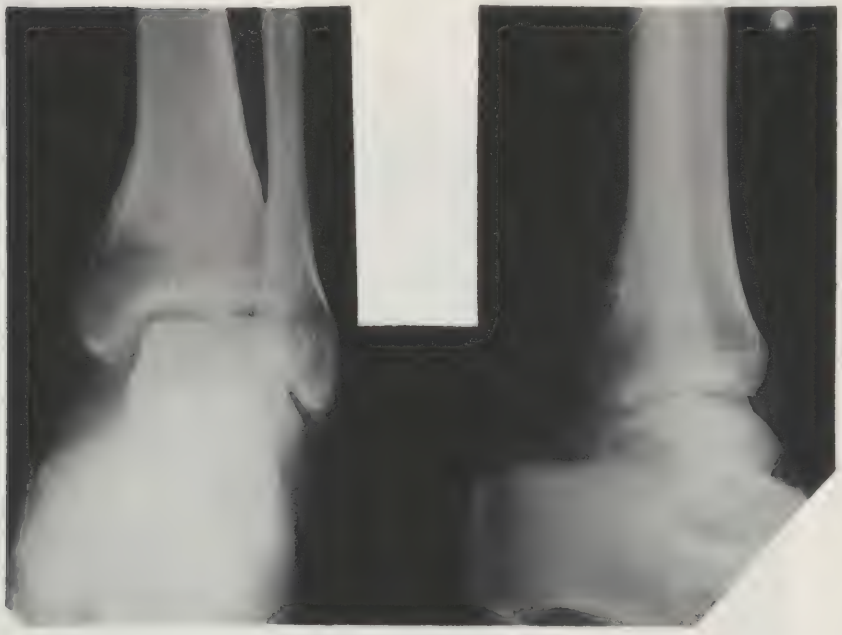
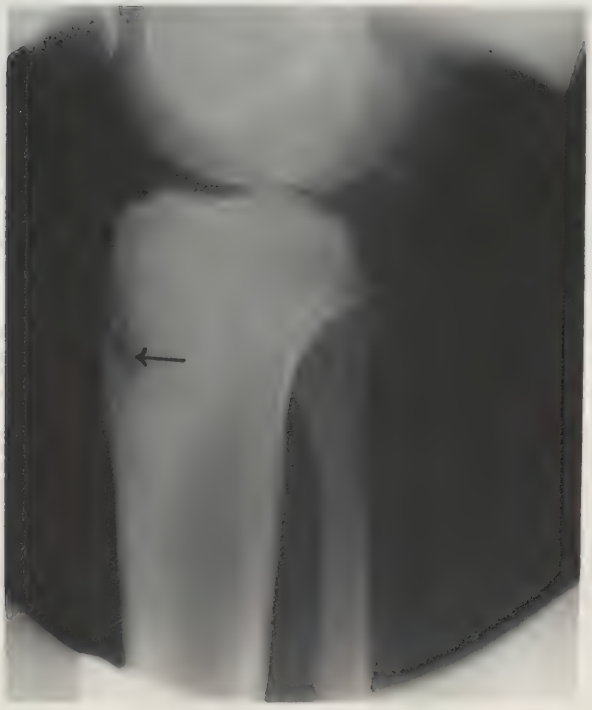


Fig. 23. Secondary coccidioidomycosis (coccidioidal granuloma).
(Upper) - Destructive osteo-periosteal lesion of the medial malleolus.
(Lower) - Destructive lesion involving the tibial tubercle.





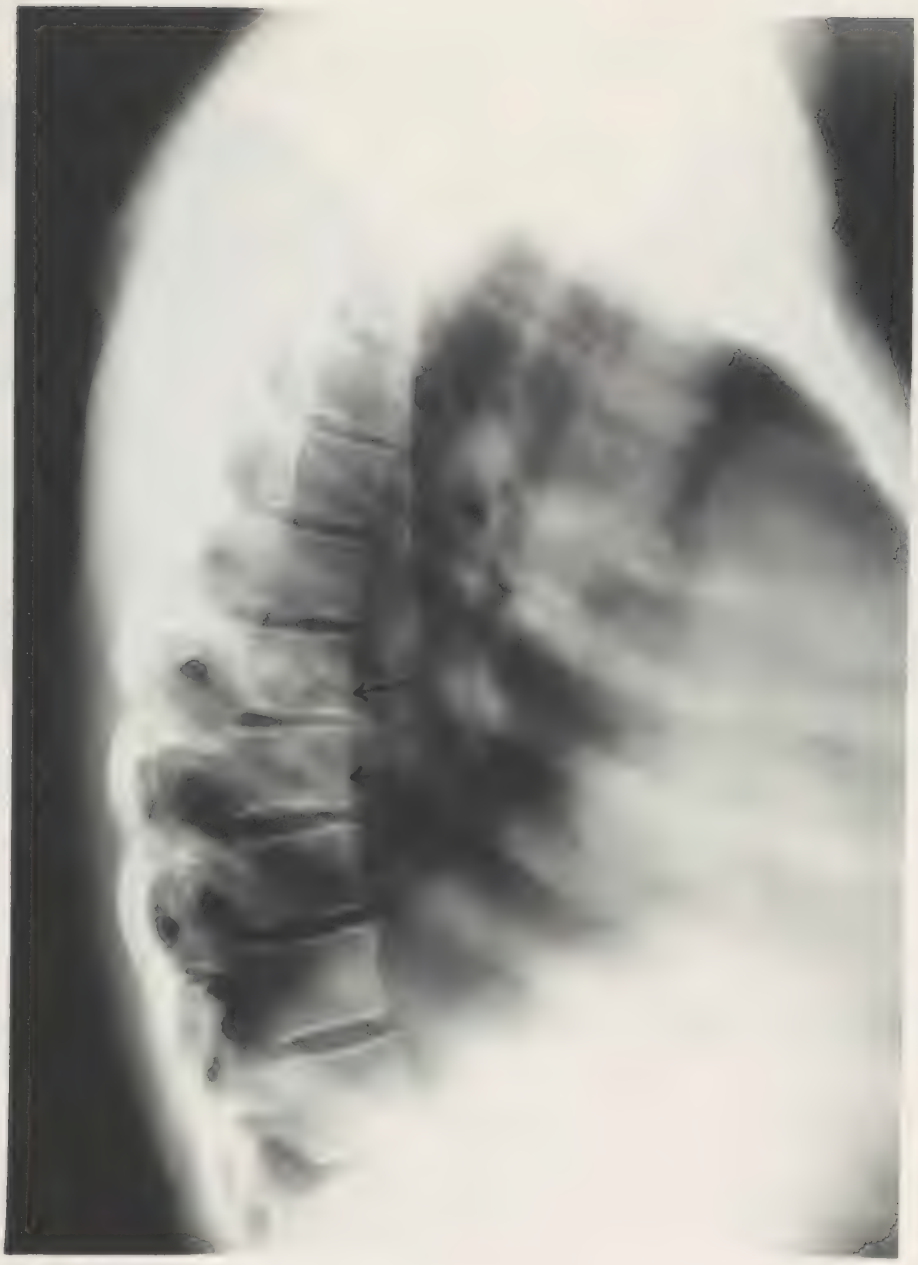
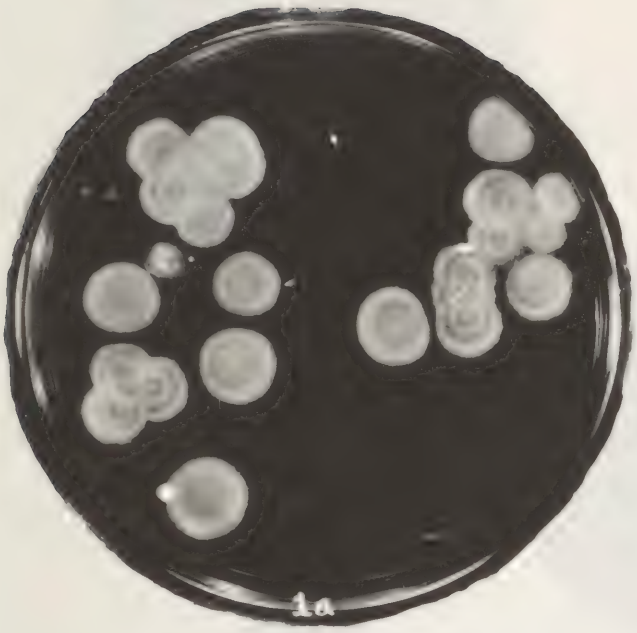


Fig. 24. Secondary coccidioidomycosis (coccidioidal granuloma). Cyst-like areas of bone destruction in the centers of mid-thoracic vertebral bodies.



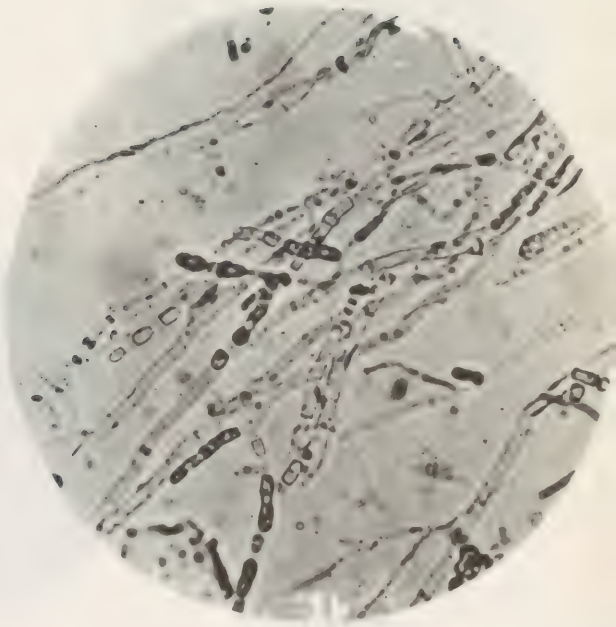


Figure 1 a

Sputum culture of C. immitis on Sabouraud's medium, showing white, cottony fungus growth.

Figure 1 b

Microscopic appearance of old culture of Coccidioides immitis showing fragmented chlamydospores. This is the infective form of the fungus occurring in nature.

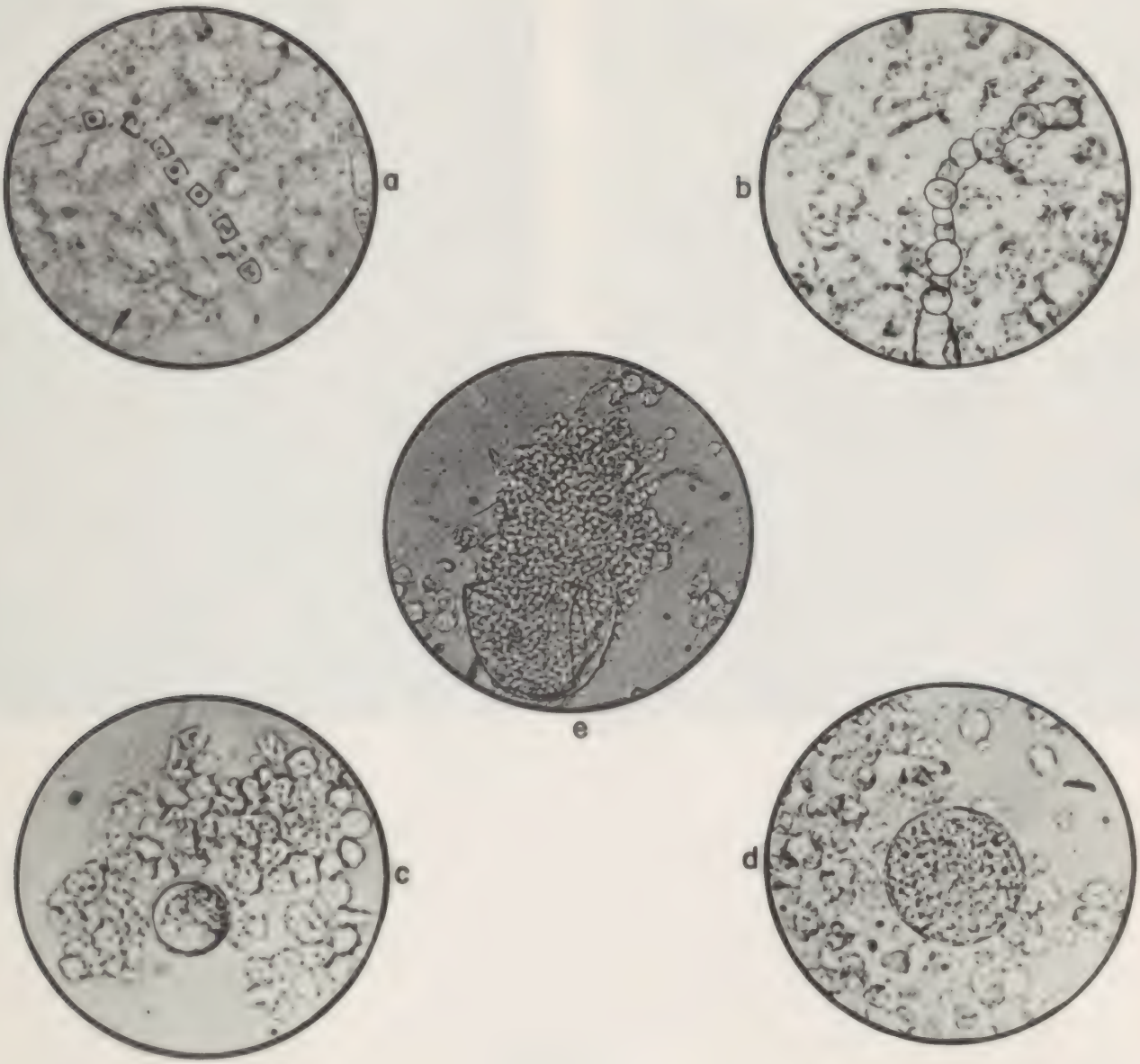
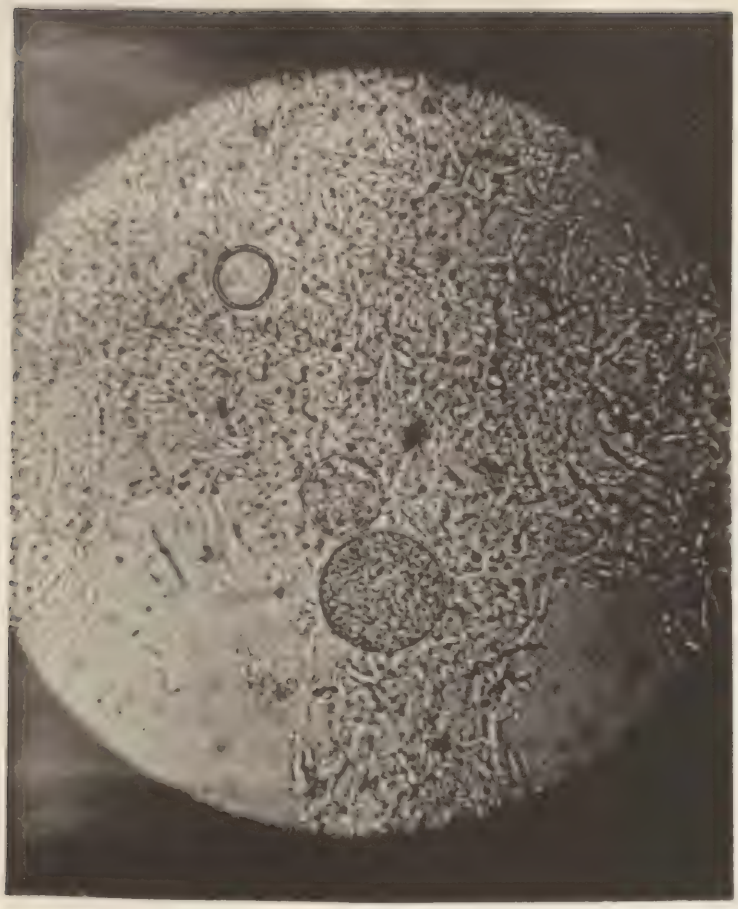


Figure 2
Development of spherules.

a. Chlamydospores in tissue.
b. Chlamydospores rounding up to form spherules.
c. Protoplasm appearing within the spherule.
d. Protoplasm divides into endospores.
e. Mature spherule ruptures, releasing endospores. Endospores are carried by lymphatics or blood stream. Each endospore increases in size and becomes mature spherule (repeating stages c, d and e.).



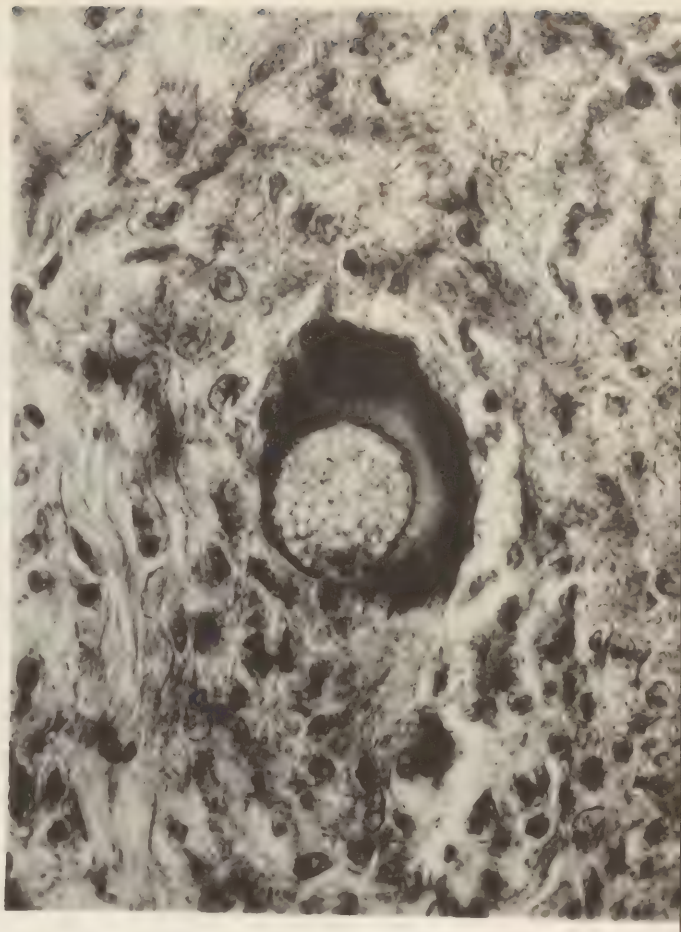


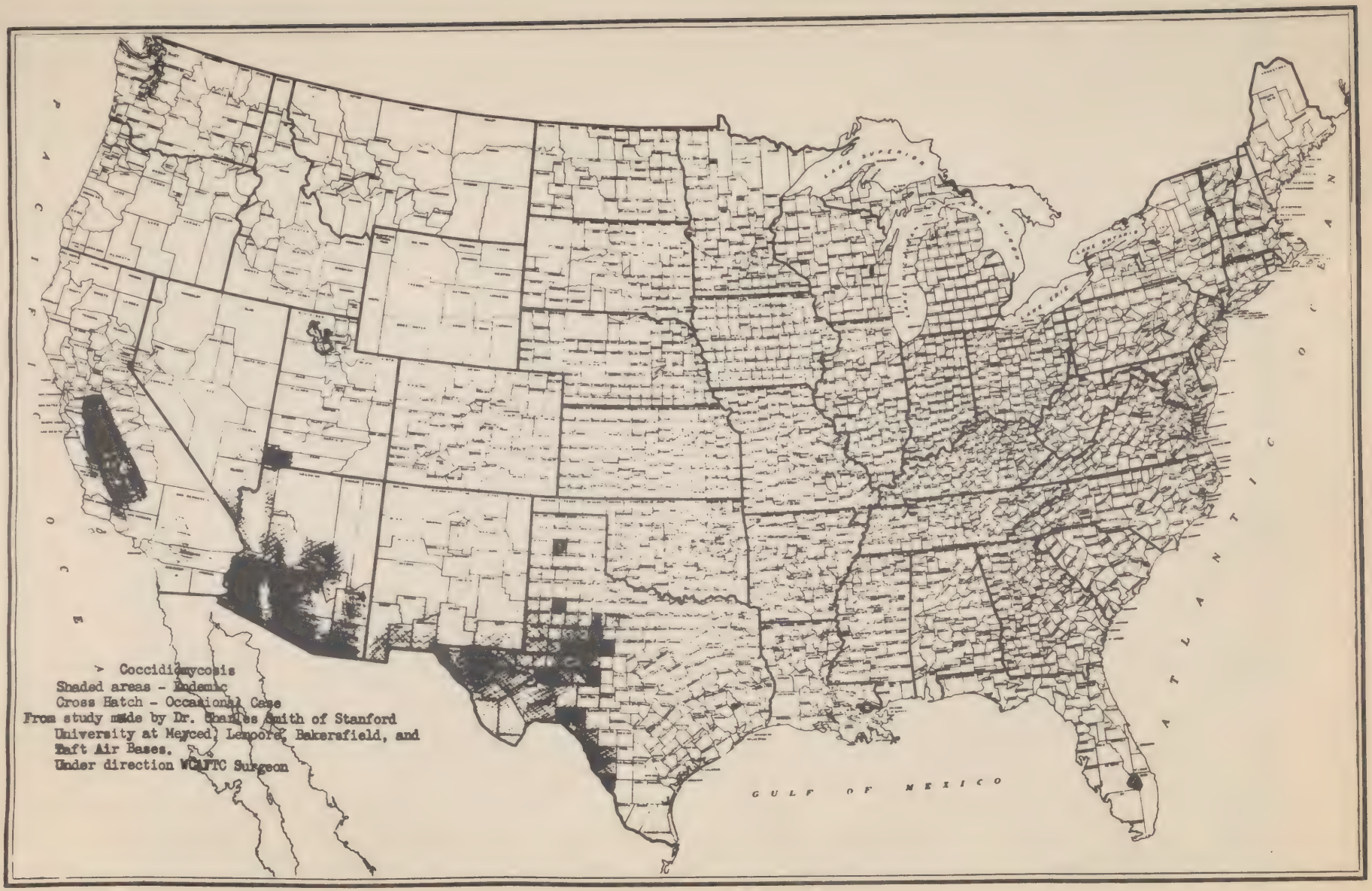
Figure 3

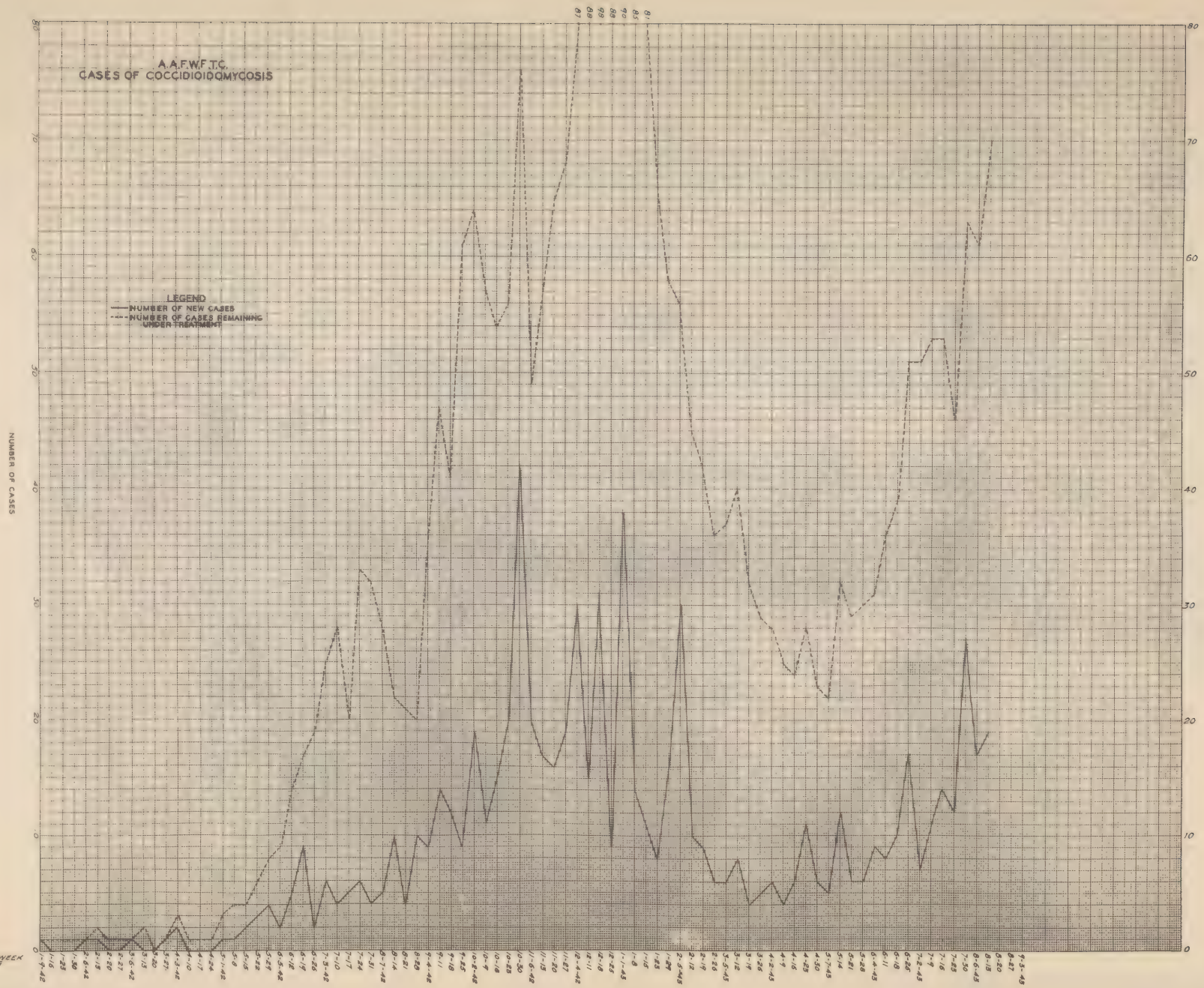
a. Spherules in coverslip preparation. This shows a double contoured spherule without protoplasm, one with undifferentiated protoplasm and a mature spherule with characteristic endospores.

b. A tissue section of coccidioidal granuloma showing a characteristic mature endosporulating spherule within a giant cell.

Figure 1 a

Sputum culture of C. immitis on Sabouraud's medium, showing white, cottony fungus growth.


PACIFIC OCEAN
ATLANTIC OCEAN
GULF OF MEXICO
Coccidiomycosis
Shaded areas - Endemic
Cross Hatch - Occasional Case
From study made by Dr. Charles Smith of Stanford
University at Merced, Lemoore, Bakersfield, and
Taft Air Bases.
Under direction WCAFTC Surgeon


A.A.F.W.F.T.C.
CASES OF COCCIDIOIDOMYCOSIS
LEGEND
NUMBER OF NEW CASES
NUMBER OF CASES REMAINING UNDER TREATMENT
NUMBER OF CASES
FOR THE WEEK ENDING

ARMY AIR FORCES WESTERN FLYING TRAINING COMMAND

Cases of Primary Coccidioidal Infection

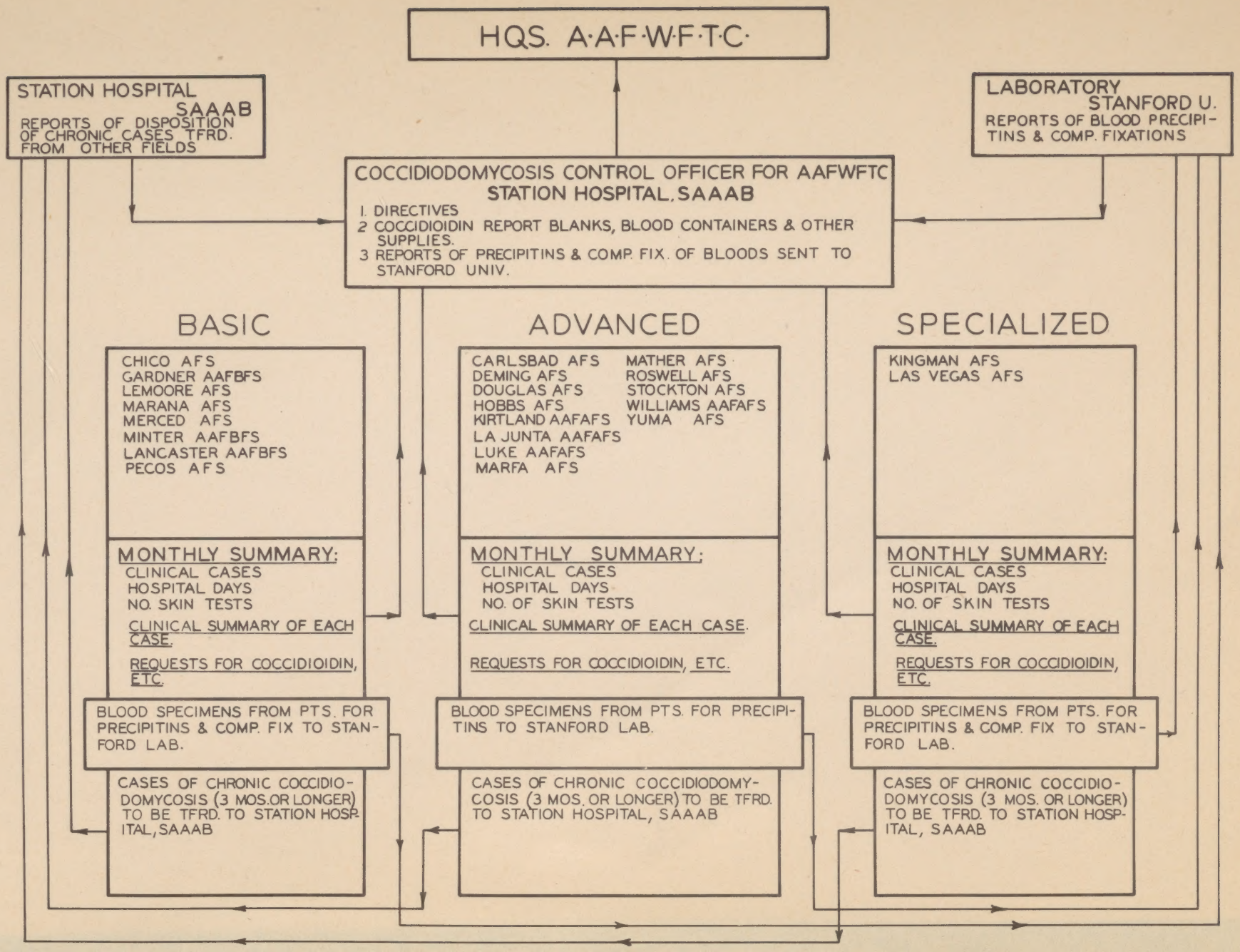
AGE	Date of arrival in the area	Date of the onset of disease	Length of time in camp (days)	Date of the discharge from the hospital	No. of days Hospitalized	SYMPTOMATOLOGY								
						head-ache	cough	mal-aise	joint pains	anor-exia	chill	back ache	night sweat	Skin Lesions
18	10/4/41	11/4/41	30	12/5/41	30	+	+	+						
19	7/8/41	9/3/41	56	9/17/41	2	*		+						
19	8/16/41	11/24/41	99	12/3/41	7	*	+	+						
19	8/1/41	6/21/42	321	8/1/42	40	+								*
19	11/25/41	12/25/41	30	1/29/42	28	*	+	+			+	+		+
20	2/1/42	7/9/42	159	8/7/42	29		+	+		+				
20	6/9/41	11/19/41	160	11/28/41	18		*			+				
21	5/10/41	8/10/41	96	8/27/41	17	*	*	+		+				
21	6/21/41	4/21/42	300	5/29/42	39			+						+
21	1/1/42	3/24/42	84	5/15/42	52		+	+		+				
21	4/26/42	6/11/42	47	8/13/42	62	+	+	*		*	*	*		
21	7/1/41	10/23/41	113	11/1/42	8		+	+		*	+	*	+	
21	9/15/41	1/27/42	132	3/3/42	36	+	*	+		+	+			
22	9/1/41	9/29/41	28	10/20/41	21	+	+	*						
22	9/13/41	10/24/41	41	11/24/41	26	*	+	+						*
22	3/1/42	7/9/42	129	8/10/42	29									+
22	3/21/42	6/2/42	72	7/17/42	45	*		+		+				
22	8/1/41	3/25/42	235	7/15/42	110	*	+	+	+	+	+	+	*	
22	2/1/42	5/1/42	90	6/18/42	47		+	+		+	*	+		
22	1/1/42	7/12/42	222	8/7/42	25	+	+	+		+				
22	1/6/42	3/5/42	59	5/14/42	69	*	*	*	+	+	+	*	*	
22	7/10/42	10/31/42	111	11/16/42	16	+	+	+		*	+	*	+	
22	8/5/41	1/1/42	146	1/20/42	19	*	+	+	*	+	*		+	
23	7/11/41	10/23/41	102	11/22/41	26	+		+						
23	4/23/42	5/20/42	27	6/9/42	19			*		+			+	
23	3/10/42	5/28/42	68	7/29/42	61		*	*		*	+	*	+	+
23	8/5/41	11/1/41	85	11/19/41	18		+	+			+			
23	11/3/41	12/8/41	25	12/23/41	15			+		+	+			
23	11/1/42	5/28/42	208	6/12/42	14	+	+		*	+				+
23	3/10/42	5/28/42	78	7/29/42	60		+	+		+				
24	7/7/41	9/20/41	73	11/21/41	25	*	+	+						+
24	1/1/42	7/21/42	201	8/1/42	10		*	*		+				+
24	1/16/42	6/29/42	191	7/29/42	30	*	*	*		*		+		
24	12/25/41	1/16/42	21	1/29/42	13	+		*	+			+		
24	8/5/41	3/24/42	229	4/25/42	30	+	+	*	+	*				
24	1/16/42	6/29/42	163	7/29/42	30	*	*	*		+		+		
25	4/7/42	7/3/42	86	8/25/42	52	*	+	*		+			+	
25	7/1/41	5/3/42	333	6/7/42	34			*	*		+			*
26	6/3/41	5/20/42	412	7/15/42	55	*	+	*		+		*	*	
26	(1/16/42 for a period of 16 days....)													
	(4/1/42	5/6/42	25	8/13/42	97		+	*		+		*	+	
26	8/6/42	11/23/41	107	1/8/42	45		+				+		+	+
26	8/5/41	3/17/42	222	4/28/42	41	*	*	*	*	+		*		
26	6/1/41	4/15/42	285	4/28/42	13	+		*		+	*		*	
27	5/22/42	8/10/42	78	8/20/42	10	*	*	*	+	+	+	*	*	
27	7/12/42	7/15/42	3	8/19/42	34			*						
31	7/1/42	7/17/42	17	8/1/42	13			+		+				
31	3/7/42	4/30/42	53	5/30/42	30		*	*		+				
32	3/1/42	5/12/42	72	8/3/42	81	*	**	*		*				
33	8/16/41	9/16/41	30	11/29/41	71		*	*	*					*
36	3/13/42	6/2/42	79	7/13/42	41	*	+	*		*				
TOTAL 50 CASES					1749	30	37	45	10	33	16	15	13	12
PERCENT OF CASES						60%	74%	90%	20%	66%	32%	30%	26%	24%

REMARKS: The average length of time hospitalized was 35 days. Of the 50 cases presented, 62% or 31 cases were hospitalized for a period of 35 days or less; 86% or 43 cases were hospitalized for a period of 60 days or less. The minimum period of hospitalization was 2 days, the maximum period 110 days.

The average time elapse between the date of arrival and the onset of the disease was 121 days. Of the 50 cases presented 64% or 32 cases contracted the disease 121 days or less after arrival into the area.

In the accompanying chart the cases were taken purely at random from among those cases at Bakersfield and Gardner Field, California.

* This case stated that he had had a cough for years.


HQS. A·A·F·W·F·T·C·
STATION HOSPITAL SAAAB
REPORTS OF DISPOSITION OF CHRONIC CASES TFRD. FROM OTHER FIELDS
LABORATORY STANFORD U.
REPORTS OF BLOOD PRECIPITINS & COMP. FIXATIONS
COCCIDIODOMYCOSIS CONTROL OFFICER FOR AAFWFTC
STATION HOSPITAL, SAAAB
1. DIRECTIVES
2 COCCIDIOIDIN REPORT BLANKS, BLOOD CONTAINERS & OTHER SUPPLIES.
3 REPORTS OF PRECIPITINS & COMP. FIX. OF BLOODS SENT TO STANFORD UNIV.
BASIC
CHICO AFS
GARDNER AAFBFS
LEMOORE AFS
MARANA AFS
MERCED AFS
MINTER AAFBFS
LANCASTER AAFBFS
PECOS AFS
ADVANCED
CARLSBAD AFS
DEMING AFS
DOUGLAS AFS
HOBBS AFS
KIRTLAND AAFAFS
LA JUNTA AAFAFS
LUKE AAFAFS
MARFA AFS
MATHER AFS
ROSWELL AFS
STOCKTON AFS
WILLIAMS AAFAFS
YUMA AFS
SPECIALIZED
KINGMAN AFS
LAS VEGAS AFS
MONTHLY SUMMARY:
CLINICAL CASES
HOSPITAL DAYS
NO. SKIN TESTS
CLINICAL SUMMARY OF EACH CASE.
REQUESTS FOR COCCIDIOIDIN, ETC.
MONTHLY SUMMARY:
CLINICAL CASES
HOSPITAL DAYS
NO. OF SKIN TESTS
CLINICAL SUMMARY OF EACH CASE.
REQUESTS FOR COCCIDIOIDIN, ETC.
MONTHLY SUMMARY:
CLINICAL CASES
HOSPITAL DAYS
NO. OF SKIN TESTS
CLINICAL SUMMARY OF EACH CASE.
REQUESTS FOR COCCIDIOIDIN, ETC.
BLOOD SPECIMENS FROM PTS. FOR PRECIPITINS & COMP. FIX TO STANFORD LAB.
BLOOD SPECIMENS FROM PTS. FOR PRECIPITINS TO STANFORD LAB.
BLOOD SPECIMENS FROM PTS. FOR PRECIPITINS & COMP. FIX TO STANFORD LAB.
CASES OF CHRONIC COCCIDIODOMYCOSIS (3 MOS. OR LONGER) TO BE TFRD. TO STATION HOSPITAL, SAAAB
CASES OF CHRONIC COCCIDIODOMYCOSIS (3 MOS. OR LONGER) TO BE TFRD. TO STATION HOSPITAL, SAAAB
CASES OF CHRONIC COCCIDIODOMYCOSIS (3 MOS. OR LONGER) TO BE TFRD. TO STATION HOSPITAL, SAAAB

2683—Santa Ana—8-30-43—550